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Report of the ANIMAL PROCEDURES COMMITTEE for 1993

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Report of the Animal Procedures Committee for 1993

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MEMBERSHIP OF THE ANIMAL PROCEDURES COMMITTEE AS AT 31 DECEMBER 1993

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MR MARTIN J HILL
MISS MARGARET SMITH } *Secretaries*

1 Introduction

1.1 The Animals (Scientific Procedures) Act 1986 regulates *any experimental or other scientific procedure* applied to a vertebrate animal or Octopus vulgaris 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. Two-third of the members must be medical practitioners or veterinary surgeons or qualified or experienced in a biological subject relevant to the work of the Committee. 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. At least half the members must not have held any licence under the Act or under the Cruelty to Animals Act 1876 within the last six years (i.e. must not have been directly involved in animal experimentation).

1.4 The membership of the Committee as at 31 December 1993 is shown on page iv. During the year Lord Nathan resigned after three years as Chairman. He took the view that the Committee had become more pro-active and required a greater commitment of time than when he had been appointed. Dr Roger Brimblecombe, Dr Henry Carter and Professor Peter Venables left the Committee on completion of their terms of appointment. We should like to record our gratitude to Lord Nathan, Dr Brimblecombe, Dr Carter and Professor Venables for the contributions they made to the work of the Committee.

1.5 In October, the Home Secretary announced the appointment of Professor Margaret Brazier, Professor of Law at the University of Manchester and a member of the Committee since 1990, as the new Chairman.

Business of the Committee

1.6 The Committee met on five occasions during 1993, including one special meeting to discuss non-human primates. Although the full Committee met on fewer occasions than in 1992, the continuation of detailed work on its review of regulatory toxicity testing through a sub-committee and its review of non-human primates by a working group meant that members have been expected to make a substantial commitment to the work of the Committee and to ensuring that the many issues surrounding the use of living animals in scientific procedures are fully and properly considered. In addition, the Research and Education and Training Sub-Committees continued to meet regularly.

1.7 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 and last year we noted that the Home Office was seeking to relieve the Secretary of some other 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. The necessary changes took place during 1993.

Amendment to the Animals (Scientific Procedures) Act 1986

1.8 In chapter 3 of the 1992 report, the Committee reported on its consideration of the case for extending the controls of the 1986 Act to cephalopods and noted that the Home Secretary had accepted the majority opinion of the Committee that the protection of the Act should be extended to *Octopus vulgaris*. The necessary amendment to the Act was made by order which came into force on 1 October 1993.

1.9 At the same time, the opportunity was taken to add quail (Coturnix coturnix) to the list of animals in Schedule 2 to the Act (animals to be obtained only from designated breeding or supplying establishments).

1.10 Regulations were also made to the effect that project licences issued under the 1986 Act can authorise the use of animals recognised as belonging to endangered species only if the purposes of the programme of work specified in the licence are either research aimed at preservation of the species in question or essential biomedical purposes where the species in question exceptionally proves to be the only one suitable for those purposes.

Developments in Europe

1.11 In paragraph 9.4 of the Committee's annual report for 1992, we recorded that the United Kingdom Government had secured political agreement on a common position on the Sixth Council Amendment to the EC Cosmetics Directive 76/768/EEC. (Cosmetics being defined as any preparation or substance intended for placing in contact with the various external parts of the human body or the mouth and not limited only to beauty products.) On 14 June, the Sixth Council Amendment to EC Cosmetic Directive was adopted. This provides for an end to the marketing of cosmetic products containing ingredients or combinations of ingredients tested on animals after 1 January 1998, with a provision for the ban to be postponed in specific cases if and only if validated alternative testing methods are not available. The Committee welcomed this step towards a reduction of a number of animals used in scientific procedures.

Campaigns about the use of animals in scientific procedures

1.12 At the beginning of 1992, the British Union for the Abolition of Vivisection (BUAV) sent to the Home Office a report and video material alleging that the controls on the use of living animals in research had not been properly applied at Wickham Research Laboratories. The report was based on information obtained by a BUAV member who worked in the Laboratories as an animal husbandry technician between July and October 1992. The main allegations were: systematic falsification of test data; poor training in methods of euthanasia, and in handling of animals in other routine animal house tasks; poor state of caging and equipment, including breaches in the Code of Practice; poor veterinary oversight and records; conflicts of interest in respect of the Managing Director's role as Named Veterinary Surgeon (NVS) and that of another Director as Certificate Holder; unnecessary animal testing, in cases where UK regulatory authorities did not require animal tests; and illegal or unauthorised re-use of animals.

1.13 Home Office Ministers directed the Inspectorate to carry out an investigation. The Medicines Control Agency also took action on matters where it had responsibility. The Committee was extremely concerned at the allegations made and was kept informed of the results of the investigation, having the opportunity to

comment on the Inspectorate's findings. The Committee congratulated the Inspectorate on the thoroughness of their report and for the way in which the authenticity of the evidence had been researched. The Committee expressed concern over the possible conflict of roles highlighted by the allegations. As a result it was agreed that the potential for conflict would be a topic for future discussion (See paras 8.7-8.9).

1.14 In the light of the Inspectorates findings it was agreed that the Home Office had taken firm, and appropriate, action where requirements of the 1986 Act had been infringed. The Committee welcomed the decision by the Home Office to discuss some of the issues raised fully with representatives of the BUAV. In response to a Parliamentary Question from Sir John Wheeler JP MP (Westminster North) the Home Office Minister, Charles Wardle Esq MP, replied:

> *The Home Office Animals (Scientific Procedures) Inspectorate and the Medicines Control Agency have investigated allegations made by the British Union for the Abolition of Vivisection (BUAV) into procedures and practices at Wickham laboratories.*
>
> *The investigation did not find substantiated some of the principal allegations against Wickham, but it did disclose poor local management, resulting in lax attitudes and practices among certain staff. These included a readiness to falsify test and environmental data on occasions. There was also one case of unnecessary animal use. Some aspects of the technical training were unsatisfactory: initial training was poorly structured and unrecorded and left some basic gaps in coverage. The system also lacked formal assessment of competence before unsupervised tasks were allocated to new employees.*
>
> *My right hon. and learned Friend has concluded that direct responsibility for the failures detected by the investigation lies with the individual who was line manager for the named day-to-day care person at the time to which the BUAV allegations relate, and who was himself named day-to-day care person at the time of the Home Office investigation. My right hon. and learned Friend has directed that he be replaced as named day-to-day care person and deputy project licence holder, and that his personal licence be revoked. In addition, the individual who was named day-to-day care person at the time of the BUAV investigation has been warned that particular attention will be paid to her current skills and knowledge if in future she should apply for a personal licence. A number of other members of Wickham staff have received letters of admonition, reminding them of the importance of a proper understanding of their responsibilities and obligations under the legislation.*
>
> *In addition to action in respect of individuals, my right hon. and learned Friend has directed:*
>
> > *that Wickham agree with the inspectorate a formal training scheme for all animal unit staff, including full records of training given and an assessment of expertise for specific tasks being made from the beginning of each individual's employment:*
> >
> > *that Wickham's standard operating procedures relating to the care, husbandry and euthanasia of animals should be revised to the satisfaction of the inspectorate and to reflect best current practice.*
>
> *It has been made clear to Wickham that a serious view has been taken of the lapses which this investigation has revealed, and that Wickham's operation will be subjected to particularly close scrutiny in the future. The Animal Procedures Committee has been informed of the outcome of the investigation, and has endorsed the action taken.*
>
> *Other allegations made by the BUAV were not substantiated, and the inspectorate had reservations about some of the evidence presented in support of the allegations. In particular, the investigation did not find that there had been unauthorised re-use of animals, or that animal suffering had resulted from poor accommodation, or that problems had arisen from a potential conflict of interests among the senior management at Wickham. On the latter point, however, the Animal*

Procedures Committee has decided to look in general terms at the conflicts which may arise when the posts of certificate holder, project licence holder and named veterinary surgeon are not all held by separate individuals.

The BUAV alleged that unnecessary animal testing took place. I am satisfied, however, that all the work carried out at Wickham was properly licensed under the Act. The general issue of animal testing performed to satisfy the requirements of regulatory authorities is currently being examined by the Animal Procedures Committee, and I look forward to receiving its advice.

Finally, I understand that the Medicines Control Agency's conclusion is that although there were operational and procedural deficiencies at Wickham, they do not call in question the validity of the particular tests, nor do they raise doubts about Wickham's continued operation as a contract research establishment. A range of improvements has been insisted upon by the agency and it will be keeping the situation under close review.

1.15 In the Committee's report for 1992 reference was made at paragraph 7.14 to BUAV criticism of research programmes involving non-human primates. The Home Office analysis was considered by the Committee which focussed on BUAV concerns about the lack of information provided in published material, about the background to research, including type and numbers of animals used. Experience amongst members differed but it was agreed that the Home Office had no authority to control the nature and content of scientific publications.

1.16 The Committee was kept informed of campaigns launched by anti-vivisection groups. The Committee fully appreciates the public concern about the use of animals in scientific procedures and will continue to take very seriously the issues raised in their discussions concerning animal use.

2 Operation of the Animals (Scientific Procedures) Act 1986

Numbers of certificate and licence holders

2.1 During 1993, 8 certificates of designation, 1444 project licences and 2779 personal licences were issued under the Act in Great Britain. Of the project licences, 614 were assessed as being of mild severity; 743 were assessed as being of moderate severity; and 21 were assessed as being of substantial severity. The remaining 9 project licences, where the work was with terminally anaesthetised or decerebrate animals, were unclassified.

2.2 In Northern Ireland, 33 project licences and 72 personal licences were issued. Of the project licences, 15 were assessed as being mild; 15 moderate; and 3 were unclassified. No certificates of designation were issued.

2.3 On 31 December 1993, in Great Britain, there were 334 certificates of designation for scientific procedures establishments; 11 certificates of designation for establishments breeding and supplying animals for use in scientific procedures; 4083 project licences; and 16,823 current personal licences. In Northern Ireland, there were 19 certificates of designation, of these 11 were for scientific procedure establishments; 7 for scientific procedures/breeding and supplying establishments and one for a scientific procedure/breeding establishment. There were 169 project licences and 472 current personal licence.

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 level 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 expected to cause. It defines an upper limit of what is allowed to be suffered by 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 and substantial procedures.

2.6 **The overall severity assessment on the project** takes into account the likely adverse effects on all the animals to be used in 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 that 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 stressing that the use or non-use of anaesthetics is not a reliable indicator of severity. In the majority of procedures actually 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 1992

2.9 The Committee welcomed the continuing fall in the use of animals in scientific procedures in so far as it reflected increased use of alternatives to live animals. The total number of procedures fell from 3.24 million in 1991 to 2.92 million in 1992.

Project licence applications to the use of animals in the safety testing of cosmetics

2.10 Cosmetics testing on animals remains a matter of public concern, even though the use of animals for this purpose remains low—accounting for only 0.06% of all procedures in 1992. (The latest period of which figures are available). 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 two applications were considered. The first was concerned with a request for renewed authority for the testing of both cosmetic ingredients and finished products; the second renewed authority to test only finished products. In both instances the applicants wished to carry out animal work to provide toxicological data required by the regulatory authorities for both the manufacture and transportation of new products.

2.11 The likely 'mildness' and safety of cosmetic products can be predicted from the knowledge of the properties of their ingredients and confirmed either by human volunteer studies or by a limited range of selected toxicology studies. In both applications companies were able to keep animal use to a minimum by using the extensive data already available to them. Where requests were made to test a product this was to ensure that the combination of ingredients had not altered the safety-in use of the product.

2.12 In the first application the tests were being undertaken to meet the regulatory requirements of the EC and Japanese authorities. The Committee carefully considered and agreed both applications on the understanding that amendments would be submitted to the Committee if circumstances changed.

2.13 The Committee receive each year a summary relating to the use of animals in Great Britain on cosmetic project licences. In 1992, 2227 procedures were carried out, a 40% decrease compared with 1991. 1,830 (82%) were used in testing ingredients and 397 on testing a single finished product.

2.14 The definition of a cosmetic covers products for both beauty preparations and cleaning products or their ingredients. The figures show that in the UK, animals are mostly used for testing ingredients and those used for finished products are more commonly involved in toiletries than in beauty preparations.

2.15 The comparative figures for 1993, were 3,741 procedures, of which 3,317 related to ingredients and 424 to finished products. The types and numbers of tests are set out in the following tables:—

COSMETIC TESTING

TEST	TOTAL NO ANIMALS	INGREDIENTS	FINISHED PRODUCTS
1992			
Contact sensitisation	576	332	244
Acute oral/dermal toxicity	94	94	0
Skin irritation	66	24	42
Photo—irritation	20	20	0
Eye irritation	201	20	0
Micronucleus test	750	664	86
Teratology	40	40	0
Sub chronic/chronic toxicity	480	480	0
Toxicokinetics	0	0	0
Skin penetration	0	0	0
Photosensitisation	0	0	0
Aquatic Toxicity	0	0	0
TOTALS	2227	1830	397

COSMETIC TESTING

TEST	TOTAL NO ANIMALS	INGREDIENTS	FINISHED PRODUCTS
1993			
Contact sensitisation	977	795	182
Acute oral/dermal toxicity	186	86	100
Skin irritation	127	38	89
Photo—irritation	0	0	0
Eye irritation	50	27	23
Micronucleus test	166	166	0
Teratology	650	650	0
Sub chronic/chronic toxicity	1489	1489	0
Toxicokinetics	24	24	0
Skin penetration	12	12	0
Photosensitisation	30	0	30
Aquatic Toxicity	30	30	0
TOTALS	3741	3317	424

Note: The figures are based upon returns of procedures carried out under project licences for testing of cosmetics and reported to the Animal Procedures Committee. The reporting year does not tally exactly with the calendar year used for annual collection of data published in the Statistics of Scientific Procedures on Living Animals. For example, in the calendar year 1992, 2,164 animals were reported as being used for testing cosmetics and toiletries as opposed to 2,227 animals reported to the Animal Procedures Committee and shown in the table above.

Applications for microsurgery training

2.16 During 1992, only one application for the use of animals (terminally anaesthetised rats) in the acquisition of skills in microsurgery was referred to the Committee. This was concerned with a request for authority to train practising surgeons in microvascular techniques. The training was to be structured as a session release system, with only those who had shown competence on in-vitro materials being allowed to perform regulated procedures. The applicant had considerable experience in running such courses. The application had been completed in accordance with the Home Office Guidance notes on such applications issued in October 1991, [see Appendix III to the Committees Report for 1991] and was approved.

Applications involving the use of tobacco

2.17 The Committee noted that no work involving the administration of tobacco or its products to conscious cats or dogs has been authorised in this country since the mid-1970's. Present practice requires that project licence applications involving the administration of tobacco or its products to conscious animals are referred to the Committee for advice, while those project licence applications involving the administration of tobacco or its products to terminally anaesthetised animals are not routinely referred for advice.

2.18 Virtually all tobacco related project licence applications are concerned with the investigation of tobacco smoke as an environmental hazard or insult. Tobacco related research accounted for 0.01 per cent of all procedures in 1992. (The last year for which figures are available.) During 1993 the Committee was not asked to consider any new applications for licences involving tobacco or its products.

2.19 The Committee was asked by Advocates for Animals to consider whether they should see all project licence applications involving tobacco or its products. After some discussion of the type of application to be encompassed by a change in policy it was decided that the Committee did not wish to adopt the suggestion.

Assessment of benefit and severity

2.20 The Committee was grateful to the Chief Inspector for setting out the elements which were assessed when the benefit and severity (or cost) of a programme of work to be authorised by a project licence is considered in accordance with the requirement of section 5(4) of the 1986 Act. A copy of his note is at Appendix II.

3 Research to Reduce, Refine or Replace Animal Procedures

3.1 During 1993 the Research Sub-Committee met on three 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. The Sub-Committee was supported by Dr Richmond of the Animals (Scientific Procedures) Inspectorate who acted as a scientific adviser. The Home Office provided the Secretariat.

Budget for the Scheme

3.2 Following a temporary increase in the research budget from £253,000 in 1992/1993 to £308,000 in 1993/94, pressures on Government finance resulted in a contraction of the budget to £273,000 in 1994/95. The Committee continues to be concerned about the level of funding and has made this clear to the Government.

3.3 Whilst this contraction in the budget in future years made it unrealistic to mount an advertising campaign inviting new applicants for grants, the Committee was able to fund two new projects, as described in paragraphs 3.4 and 3.5 below. These were projects previously identified by the Research Sub-Committee as being particularly worthy of support.

New Research Grants Awarded during 1993

3.4 A grant was made to Dr Stuart Milligan of the Department of Physiology, Division of Biomedical Sciences, King's College London who had proposed a study with the long term aim of improving the housing and care of laboratory animals. The study will investigate the effects of the levels and frequencies of sounds known to be prevalent in animal facilities; behavioural and physiological responses will be monitored, and habituation and threshold levels studied. It is intended that the programme of work will identify levels and frequencies of sounds which, in the interests of animal welfare and scientific validity, should be avoided in animal facilities.

3.5 A grant was made to Dr Paul Skett of the Department of Pharmacology, University of Glasgow, as part-funding of a European multi-centre initiative to reduce the numbers of animals used in metabolism studies and toxicity testing. The long term aim is to optimize the freezing, thawing and primary culture conditions required to prepare hepatocytes from a variety of species including man for subsequent use in metabolism studies and toxicity testing. Current in vitro systems rely principally on material harvested from freshly killed animals. The availability of, and potential to use, standardised cryopreserved material would reduce the number of animals required, and allow the selection and use of cells from a species representative of the relevant human biotransformation pathways.

Completed Research

3.6 During 1993 six studies funded by the APC Research Sub-Committee were concluded. The outcome of these studies is summarized briefly in paragraphs 6.7 to 6.24 below.

Alternative Approaches to Animal Protection Studies

3.7 The Home Office and Unilever provided joint funding for a study conducted by the University of Nottingham Department of Microbiology. The aim of this study, which formed part of a larger research effort, was to further develop and

evaluate a novel intraperitoneal containment chamber as an alternative to conventional in vivo systemic bacterial challenge testing systems.

3.8 During the tenure of the award the time between chamber implantation and inoculation with bacteria for in vivo studies was optimized, and the effect of pore size on equilibrium rates was determined. The chambers were well tolerated and the animals did not suffer significant systemic adverse effects associated with bacterial growth within the chambers. It was demonstrated that the in vivo diffusion rates of proteins and antibiotics was markedly slower than the in vitro rates, and was subject to significant interanimal variation. Differences were noted between serum and chamber concentrations of antibiotics. In addition to confirming that the model has the potential to assess antimicrobial effect in vivo, the system also proved capable of producing large numbers of in vivo grown organisms for analytical and morphological studies.

3.9 The model system may have a place in antimicrobial dose ranging studies as an adjunct to conventional challenge studies, but further work is required to determine its potential as an alternative to conventional challenge models.

Publications to date

Artbuthnott, J P, Arbuthnott E R, Arbuthnott A D J, Pike W J and Cockayne A (1992) Investigation of Microbial Growth In Vivo: Evaluation of a novel in vivo chamber implant system. FEMS Microbiology Letters 100: 75–78.

Immortalised Cell Lines for Virus Diagnosis

3.10 In 1990 the Research Sub-Committee awarded a grant to the PHLS Centre for Applied Microbiological Research, Division of Biologics, to study the use of oncogene transfection to establish continuous baboon kidney cell lines with the long term aim of finding an alternative to the current need to use non-human primate primary kidney cells for the detection and isolation ofa range of human viruses from clinical specimens.

3.11 Primary baboon kidney (PBK) cells were immortalised by oncogene transfection with one of three plasmids. Established cell lines and the successfully immortalised cells were tested for virus susceptibility. No current cell line, or combination of cell lines, matches the specificity and sensitivity of PBK cells for isolation of certain viruses. Some of the immortalised cells displayed a range of virus susceptibility but not the sensitivity seen in PKB cells.

3.12 Since the study began diagnostic laboratories have been making increasing use of Rhesus macaque primary kidney cells and these appear to be even more sensitive to human viruses than PBK cells from the baboon. In addition new plasmid constructs are available which may exert their immortalizing effects by different mechanisms. Future work is likely to seek to immortalise Rhesus kidney cells with a wider range of oncogenes, and to asses the value of the resulting immortalised cell lines in virus diagnosis.

Publications to date

1. Clarke, J B et al: Animal Cell Technology—"New Cell lines for Virus Diagnosis"—Developments, Processes and Progress (Ed Spier, Griffiths and MacDonald)—Butterworth-Heinemann, Oxford) 1992, 661–663.
2. J B Clarke, C MacDonald, U Kreuzburg-Duffy and J B Griffiths: Animal Cell Technology—"Immortalized Cell Lines for Virus Diagnosis"—Products for Today, Prospects for Tomorrow (Ed Spier, Griffiths and Berthold)—Butterworth-Heinemann, Oxford) 1994 p 50–54.

The Creation of a Database: Adjuvants, Antigens and Animals

3.13 In 1990 a grant was awarded to Professor D E Stewart-Tull of the University of Glasgow, Department of Microbiology, to establish a computerized

database to allow research workers access to information which would permit appropriate protocols of minimal severity to be designed for the administration of adjuvants and antigens to animals.

3.14 A computerized database containing records based on published work and detailing the animal, the adjuvant, the antigen, the protocols and recorded adverse effects has been prepared. Sponsorship was also obtained from Blackwell Scientific Publications Ltd, the publishers of the Idealist computerized data retrieval system. The IBM PC compatible database can now be purchased by research workers, as a read only computerized database. Consideration is being given to the preparation of an Apple MacIntosh compatible version, and to the provision of the database as hard copy.

3.15 Full details of the system appeared in the EAG Letters, Newsletters From The European Adjuvant Group, Volume 7 no. 1 1994. Copies of the database have subsequently been supplied to research groups in the United Kingdom, Europe, North America and Australasia.

Refined Models of Inflammation for Use in Evaluating Novel Anti-Arthritic Drug Delivery Systems.

3.16 In 1992 a grant was made to Dr Glynn Taylor of the Welsh School of Pharmacy, University of Wales College of Cardiff, to evaluate a range of animal models of inflammation for use in research with a novel drug delivery system, with the intention of evaluating the potential to use models of lesser severity than adjuvant induced arthritis in the rat.

3.17 The novel drug delivery system evaluated by the group involved the delivery of liposome-entrapped anti-inflammatory agents. Studies were conducted using the rat subcutaneous air pouch and acute and chronic rabbit antigen-induced mono-articular arthritis models; in contrast to adjuvant induced polyarthritis these induced minimal welfare problems in the animals used.

3.18 The rat air pouch model confirmed its potential to screen for the effect of drugs on inflammatory mediators and possibly study drug pharmacodynamics. The more chronic rabbit antigen-induced mono-arthritis model can be used to determine the specificity of target drugs to this type of inflammatory focus. These models have the potential to investigate the accumulation of liposome-encapsulated drugs and other selective anti-inflammatory drug delivery systems. Work relating to the liposome-encapsulated delivery system is continuing. Publications are expected during 1994.

Evaluation of Welfare In the Husbandry of Rabbits

3.19 In 1989 the Research Sub-Committee agreed a grant to Professor David Morton of the University of Birmingham, to enable him evaluate the to welfare implications of husbandry systems current used in the UK for the housing and care of laboratory animals.

3.20 At the time of writing the final report summarizing the findings of the study has not been received by the Home Office.

Transmissible Spongiform Encephalopathies: Tissue Culture Detection System

3.21 In 1992 the Research Sub-Committee awarded a grant to Dr P M Edwards of MAFF Central Veterinary Laboratory to fund an attempt to determine the feasibility of developing a tissue culture system to reduce the need to use in-vivo testing for the detection of transmissible spongiform encephalopathy agents.

3.22 Initial work highlighted significant technical limitations with the proposed test systems, and following an internal MAFF re-organisation further work on the project came to a halt.

3.23 The residual funding has been added to that available for the funding of new work by the Sub-Committee.

4 Non-Human Primates

4.1 Last year, the Committee reported that it had established a working group to take forward a review of the use of laboratory primates. The Working Group consisted of Professors Balls and Iversen, with members of the Inspectorate acting as advisers and the Home Office providing the Secretariat.

4.2 The Working Group considered information about the use of non-human primates in research and identified a number of areas in which it would be possible to make early recommendations. The first two recommendations concern the presentation of project licence applications and were intended both to focus the mind of applicants and to assist the Inspectorate when formulating advice on project licence applications:

(i) project licence applicants should be required to include a separate section in their applications specifically explaining why primates are required in the research programme. While the special justification required by the Act may be implicit in the terms of the application, it would be preferable to have this made explicit;

(ii) in the case of old world primates the justification for using such primates should be spelt out clearly in the project licence application in view of the special concern about their use in research. If this recommendation were to be accepted by the Home Secretary and prove successful in implementation, the Working Group recommended that the process should be extended to applications involving new world primates; and

(iii) a more comprehensive statistical breakdown of primate use should be included in the annual statistics, whether as a separate table or in the commentary included in that publication.

4.3 The Animal Procedures Committee accepted the recommendations and wrote to the Home Secretary as follows:-

Laboratory Non-Human Primates

I am writing to you on behalf of the Committee to inform you of the work of the Committee on the use of non-human primates in laboratories.

2. While accepting that non-human primates are essential for certain aspects of medical research, we are committed to the view that improved knowledge and understanding of the current patterns of usage in the United Kingdom will ensure that every effort is made both to improve the quality of life of laboratory primates and guarantee that all reasonable efforts are made to reduce, refine and replace the use of non-human primates in scientific research.

Background

3. Of the total of 3.2 million procedures started in 1991 some 4,500 involved primates. There is understandable public concern about the need to use of such animals in research, a concern that the Committee shares. That concern arises from the fact that non-human primates are closest to humans in terms of evolutionary development, the complex nature of their behavioural and social interactions and the difficulty of housing them adequately. It is, however, the very closeness to humans which makes them of particular value in certain areas of research. Primates (together with dogs, cats and equidae), are accorded special protection under the terms of the Animals (Scientific Procedures) Act 1986. The Act requires that such species may only be

used in research if no other species are suitable for the purposes of the programme of research or if it is not practicable to obtain animals of any other species that are suitable for the work in question.

4. The Committee's interest in non-human primates is not new. Indeed one of your predecessors asked the Committee to consider his proposed response to the report, "The Use of Non-Human Primates as Laboratory Animals in Great Britain", jointly published by the Fund for the Replacement of Animals in Medical Experiments and the Committee for the Reform of Animal Experimentation and endorsed by the British Veterinary Association and the Royal Society for the Prevention of Cruelty to Animals. The Committee recommended that the Home Office accept and implement the majority of the recommendations in the FRAME/CRAE report and Appendix VI to our annual report for 1987 detailed the recommendations which the then Home Secretary, on the advice of the Committee, felt able to accept. Since then, the Committee has also received a joint survey by the RSPCA and FRAME on the use of non-human primates as laboratory animals in Great Britain based on research published between 1984 and 1988. The FRAME/CRAE and RSPCA/FRAME reports have provided useful background to the current work of the Committee on primates.

5. More recently the use of non-human primates in research has been the subject of renewed interest following reports by two animal pressure groups, Advocates for Animals and the British Union for the Abolition of Vivisection, questioning the justification for the use of primates in particular programmes of research. The latter group also mounted a campaign against the international trade in primates for research following the submission of a report to the Home Office on the conditions under which some imported primates were kept in the UK. While the Committee was kept informed of the Home Office's reactions to the criticisms in these reports, and is aware that the allegations made by Advocates for Animals were not substantiated by Home Office investigations, it has been keen to consider the issues which they raised, rather than involve itself in discussion of the research projects criticised. It appeared to us that it would be better use of our time, to consider the principles which should govern the treatment of primates in research, and the circumstances in which such use remains justified, rather than engage in detailed debate about projects long since authorised and carried out.

6. The Committee itself plays a role in advising on certain project licence applications involving primate use. Should a project licence application be submitted involving the use of non-human Hominoidea (i.e the gibbon, the orang-utan, the siamang, the chimpanzee and the gorilla) it would be referred to the Committee for advice. There have been no such applications since the Act came into force or for several years before that. The APC also considers any application which involves procedures on primates of substantial severity, regardless of the proposed overall severity assessment of the project licence. Such applications are relatively rare, but the Committee is given the opportunity to offer its advice to the Home Office on those which may arise from time to time.

7. In order to carry our work forward we have established a small working group of two Committee members, together with two Home Office Inspectors. We should like to record our gratitude to the Inspectorate for the work it has done in providing background information for the Working Group. This has been of particular value in informing the Working Group about the current use of non-human primates in research in this country. The Committee has also met with representatives of the All Party Parliamentary Animal Welfare Group who outlined to the Committee the aspects of primate research which caused them particular concern. We envisage that the Committee's interest in laboratory use of non-human primates will be taken forward in a rolling programme which will look at specific issues, and subject to your views, we would intend to make recommendations to you as and when they have been considered and agreed by the Committee.

Emerging recommendations

8. The Committee has already considered and agreed several recommendations resulting from the work of the Committee's Working Group. These are set out below.

9. All project licence applicants are required to provide special justification for the proposed use of non-human primates in their programme of research. In a number of project licence applications this special justification will be implicit. We recommend that applicants should be required to include a specific heading in section 18 of the project licence application to explain clearly why only non-human primates, as opposed to any other species, (including Man where appropriate), are considered essential in any programme of research and, where applicable, why the use of old-world rather than new-world primates is proposed. The purpose of this recommendation is to make clear to all concerned the special considerations relating to these species, to focus the minds of applicants on their proposed use of primates, and to ensure that they have considered all possibilities for achieving the purpose of the programme of research by other means which do not involve the use of non-human primates. The recommended change will also, we think, assist the Inspectorate in considering project licence applications by ensuring that applicants have given careful thought to these issues before any draft application is submitted. We also recommend that any procedures to be carried out using primates should be described in separate protocol sheets (section 19a and b) of the project licence applications. Non-human primates should not be grouped with other species in such descriptions, even when the protocols to be used are similar. The purpose of this recommendation is to describe the details of those procedures involving non-human primates which will be specific to that species so that the extent of each procedure and the expected consequences are clearly defined.

10. Following on from the recommendations above, and in order to strengthen the controls, we also recommend that for toxicology project licence applications proposing the use of old world non-human primates (e.g macaques and baboons), in procedures of more than mild severity, the justification for using such primates should be set out clearly in the application on a study by study basis in view of the special concern about their use in toxicological research. This will mean progressive additions to the project licence as new studies become necessary. It is recommended that the Inspectorate should examine the specific protocol relating to each material to be investigated where more severe toxic effects is predicted. By knowing the type of compound to be tested and the likely effect on the animals, the Inspectorate will be better placed to advise whether the use of primates is justified. We further recommend that if this recommendation is accepted and proves to be feasible and successful in implementation, such closer scrutiny should be extended to applications involving new world primates (mainly marmosets, but also tamarins, squirrel, owl and spider monkeys). One of our specific concerns about the use of primates in contract research establishments is that the sponsor, which may be an overseas company, may not always inform the contract research establishment about the nature and proposed use of the substance to be tested. This adds to the difficulty in weighing the potential benefit against likely suffering on which you make a judgement on the advice of the Inspectorate under section 5(4) of the Act.

11. We also recommend that more detailed collated data on primate use should be included in the Annual Statistics of Scientific Procedures on Living Animals, Great Britain or, alternatively in our annual reports. We believe such information would provide useful background for a better informed debate on non-human primate use in UK research. The Committee has been given the opportunity to consider further information on work carried out under project licence authority, provided for the Committee by the Inspectorate. This should keep us well informed of current primate use and future developments.

12. Finally, we should like to turn to the question of the supply of non-human primates for research. It has been government policy for a number of years to recommend the use of captive bred rather than wild-caught non-human primates in UK laboratories. The Inspectorate's recent survey indicates that the Home Office has been successful in implementing this policy and it is likely that virtually all non-human primates currently in use for research have been bred in captivity. However the issue is one of great public concern and further action is required. At its next meeting, the Working Group intends to focus upon the availability and quality of captive-bred animals from Europe and non-European sources. It expects to be confident to advise the Committee to recommend a practical strategy, which can be implemented speedily,

that will obviate the need to use wild-caught non-human primates unless there is a special scientific purpose or some presently unforeseen requirement which can be strongly justified; and which will not impede essential academic or commercial research and development.

13. As is normal practice, we would propose to include the text of this letter and your reply in our next annual report.

Future work of the Working Group

4.4 As the letter to the Home Secretary explains, the Working Group identified a number of other areas which the Committee agreed it should consider further. It is now focusing on the use of wild-caught and captive bred non-human primates. The Working Group is aware that it has been Government policy that captive bred rather than wild-caught animals should be used and have been informed by those involved in the supply of animals for research that it is no longer the practice to provide wild-caught non-human primates.

Project Licences

4.5 The Committee now receives information on all new project licences which allow for the use of non-human primates, and are consulted about any licence applications involving procedures of substantial severity before a decision is taken on issue. Members of the Working Group receive more detailed information about each licence in order to give guidance, if required. During 1993, 28 project licences involving non-human primates were issued; 19 of these included New World monkeys (mainly marmosets and tamarins) and 15 Old World monkeys (macaques and baboons).

5 Regulatory Toxicity Testing

5.1 Last year, we reported on the manner in which the Sub-Committee appointed to consider the issues arising from the use of living animals in regulatory toxicity testing was handling its remit and noted that the Sub-Committee intended to report to the main Committee in 1993.

5.2 The Sub-Committee met on 7 occasions during the year but because of the complex nature of the issues was not able to finalise its report and recommendations until January 1994, outside the period covered by this Report.

5.3 The Committee would like to express its appreciation to Dr Donald Straughan, who acted as expert adviser to the Sub-Committee until his retirement from the Inspectorate in September and made an invaluable contribution to the development of the Sub-Committee's thinking on the subject.

6 Education and Training

6.1 Chapter 6 of the Committee's annual report for 1992 set out developments in the education and training of project and personal licence holders and the Home Office Statement of Policy was set out at Appendix IV.

6.2 The Policy requires that all training programmes are accredited under schemes recognised by the Home Office. The purpose of accreditation is to achieve common and high standards for animal use which, inter alia, promote best practice in animal welfare and use and command public and parliamentary support. These aims can best be met by having accreditation of training programmes carried out by independent bodies which are not associated either with the body providing the training or with the Home Office as the regulating body.

6.3 While the Home Office would have preferred one single accrediting body because it would have avoided the issue of the Department's competence to adjudicate on the merits of different schemes, it accepted that this was not a sufficient ground for refusing to recognise more than one scheme.

6.4 The Animal Procedures Committee agreed that it would be inappropriate for the Home Office to limit the number of accrediting bodies and accepted that, given the range of expertise available to the Committee and its function as an independent adviser to the Secretary of State, it would be right for the Committee to advise the Secretary of State on acceptance of accreditation schemes. Accordingly in 1993, it appointed a Working Group with a remit to consider all applications for recognition of accreditation schemes by the Home Office and to offer advice to the Home Secretary via the Animal Procedures Committee.

6.5 The Group considered and agreed the criteria to be used for determining the acceptability or otherwise of an accreditation scheme. These are:-

(i) accreditation of training programmes should be carried out by independent bodies which are not directly associated with the body providing the training;

(ii) the proposed scheme should have a syllabus which at least meets the requirement set by the Home Office in its policy statement of February 1993;

(iii) the means of assessment of trainees should be such as to ensure that participants have adequate understanding of their responsibilities and sufficient knowledge of animal husbandry that good welfare practices will be assured;

(iv) the scheme should be able to cater for a wide variety of users and species unless it is restricted to specific user groups; and

(v) the scheme should set out clearly how it will be administered, how courses will be supervised and monitored, how long accreditation will last and how trainees will be notified of their performance in the course.

6.6 The Working Group considered two applications and on their recommendation the Animal Procedures Committee advised the Home Secretary to approve applications from the Institute of Biology and the Universities Group for the Accreditation of Training as approved bodies.

6.7 The Animal Procedures Committee has approved the proposals of the Working Group for continuing oversight of accreditation schemes and training courses. Members of the Working Group or other members of the Committee will attend meetings of the supervisory bodies operating the schemes as observers to satisfy themselves that appropriate arrangements are in place for monitoring accredited training programmes. They will also attend training courses on occasions to

satisfy themselves that acceptable standards are being obtained and that assessment procedures are adequate.

6.8 The Committee has noted the positive response to the Home Office statement of policy from many people involved in activities controlled by the Act and welcomes the high level of commitment to training within most designated establishments.

6.9 The effectiveness of the new arrangements will be greatly helped by the publication of the Directory of Animal Research Training Courses. The Committee is grateful to the Research Animal Liaison Council for preparing the Directory and ensuring that it is kept updated.

7 Infringements

7.1 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.

7.2 The Committee receives a report of each infringement where a determination has been made.

7.3 In 1993, 12 infringements were reported to the Committee. In one case a personal licence was revoked because of a lack of concern for the welfare of the animals and disregard for the regulations and controls under the 1986 Act. The project licence holder and the day to day care person were required to undergo further training.

7.4 Apart from this case, the Committee's main concern continues to be the degree to which infringements resulted either from an imperfect understanding of the requirements of the Act or of conditions issued under it by those concerned, or a failure of the systems of control within a designated establishment which allowed procedures to be performed inadvertently by staff without the appropriate personal or project licence authority. In most cases had the necessary authority been sought it would have been granted.

7.5 The Committee noted that a number of these cases had been brought to the attention of Inspectors by licensees as soon as they had become aware of an infringement and welcomed the openness that this reflected.

7.6 The Committee has continued to follow developments in the case reported at paragraph 3.9 to 3.11 of the Committee's annual report for 1991 and paragraph 5.7 of the report for 1992. Members have expressed their concern at the delay in reaching a final conclusion in the matter.

8 Forward Look

Regulatory Toxicity

8.1 In 1994 the Committee will be considering the report of the Regulatory Toxicity Sub-Committee. We aim for this to be published and to form the basis of consultation between the Home Office and regulatory authorities and others with an interest in regulatory toxicity.

Non-human primates

8.2 Chapter 4 records the work that has already been done but the use of non-human primates is of particular concern to the Committee and the programme of review will continue.

Draize Eye Test

8.3 The Inspectorate reported to the Committee during 1993 the outcome of a review on compliance with the Home Office Guidelines on Eye Irritation/Corrosive Tests, which had been endorsed by the Committee and issued in 1987. The Committee noted that the Inspectorate review recorded an impressive level of compliance with the guidelines and that a cautious, tiered approach appeared to be working well. No significant compliance failures were identified. The Inspectorate will be revising the Guidelines, to clarify the advice and remove ambiguities, before consulting the Committee.

Revision of Schedule 1

8.4 Schedule 1 of the 1986 Act sets out the standard methods of humane killing. Killing a protected animal in an establishment designated for the purposes of the Act is not a regulated procedure and does not require authorisation by a project or a personal licence if carried out by a Schedule 1 method. It is a condition of certificates of designation that the certificate holder shall ensure that a person competent to kill animals in accordance with these conditions is available. Methods of killing other than those included in Schedule 1 may be allowed provided they are performed by a competent person either licensed as a regulated procedure or under authority conferred by a special condition in the certificate of designation.

8.5 In 1993, the Committee considered a suggestion from the RSPCA that Schedule 1 might be repealed. The main argument being that if killing is carried out incompetently, suffering will be caused and that even when carried out competently, pain, suffering or distress will be caused on some occasions.

8.6 Repeal of Schedule 1 would result in any killing for a scientific purpose at a designated establishment being regarded as a regulated procedure. The Committee were persuaded that there continued to be a need for Schedule 1; that there were sufficient safeguards to ensure competence; and that repeal would not provide sufficient benefit to justify the additional administrative burden such a change would impose. It was noted that the Home Office were in the process of revising Schedule 1 and drafting a Code of Practice. These would be put to the Committee for comment.

Conflicts of interest

8.7 The Committee discussed the potential for conflicts of interest arising from one person combining the role of Named-Veterinary Surgeon and Managing

Director as part of its consideration of the response to the investigation at Wickham Research Laboratories Ltd (see para 1.13).

8.8 While the Committee were aware that no specific problems relevant to the 1986 Act had been attributed to conflict of interest it remains an issue of recurring concern. The potential for such conflicts would seem to be increased by the combination of roles and responsibilities in a single individual, particularly where one of the roles confers a major financial or other interest in the outcome of research programmes which may come into conflict with the best interest of animal welfare.

8.9 Theoretical conflicts of interest are implicit and inescapable in the roles and responsibilities allocated to individuals by the 1986 Act. The Committee proposes to look at the issue and to consider whether any changes in practice need to be recommended.

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 1993 for scientific procedure establishments was £120, and £108 for each personal licensee. For breeding and supplying establishments with no personal licensees, the fee was £545. 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 1993, 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. 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. This decreases the time available in which Inspectors can carry out their licensing and inspection duties.

Appendix II

ASSESSMENT OF BENEFIT AND SEVERITY

Note by the Chief Inspector, Animals (Scientific Procedures) Inspectorate

1. The assessment of benefit and severity (or cost) is a necessary prelude to discharging the duty of the Secretary of State, under Section 5(4) of the 1986 Act. To do this the Home Office Inspectorate must weigh any likely adverse effects of regulated procedures on animals against the benefits likely to accrue as a result of a proposed programme of work. The general approach of the Home Office is set out in paragraph 4.4 to 4.6 of the Home Office Guidance on the Operation of the Animals (Scientific Procedures) Act 1986.

2. This essential judgement is made on the basis of information set out in an application for a project licence (PPL) which is structured so that most of the relevant information is contained within three sections:

(i) Section 17: Background, Objectives and Potential Benefits.

(ii) Section 18: Description of Plan of Work.

(iii) Section 19: Protocol Sheet(s) (Description of the procedures).

3. By taking some liberties with mathematical notation, it is possible to illustrate the link between the severity/benefit analysis and the structure of the project licence as follows:

Cost/benefit or severity/benefit analysis should be regarded as synonymous with justification. Thus:

(i) $\text{Justification} = \frac{\text{Benefit}}{\text{Cost}}$

(ii) $= \frac{\text{Importance of Objectives} \times \text{Probability of Achievement}}{\text{Cost to animals in suffering}}$

(iii) $= \frac{\text{Background/Objectives Potential benefits} \times \text{Scientific Quality}}{\text{Adverse effects—Coping strategies}}$

(iv) $= \frac{\text{Section 17} \times \text{Section 18}}{\text{Section 19}}$ of PPL

4. The equivalence shown at 3(ii) above is a convenient starting point for an examination of the factors relevant to the cost/benefit analysis.

Importance of Objectives

5. This is determined by the general attributes of suitable objectives and the nature of any potential benefit likely to result from their achievement.

(a) General attributes:

(i) Original: new approach or fresh insight in relation to existing knowledge provided as "Background".

(ii) Realistic: not over-ambitious; achievable; specific; focused; likely to be funded.

(iii) Relevant: has links with and implications for other areas of research.

(iv) Current: relates to issues of current or developing interest or concern.

(v) Potentially beneficial: see below.

(b) Potential benefits:

(i) Human, animal and ecological benefits: improved health or welfare, plant protection, food hygiene, safeguarding of the environment.

(ii) Scientific benefits: resolution of controversies, increasing scientific knowledge.

(iii) Educational benefits: meeting educational objectives which cannot be satisfied using non-animal methods.

(iv) Economic benefits: profitability; employment; conservation of natural resources.

(v) Other: forensic enquiries.

Probability of Achievement

6. This equates with scientific quality and is both the reason and the justification for inspectors' authority to question the scientific validity of proposals on behalf of the Secretary of State. Items to be addressed include:

(i) Is animal use necessary at all? Has appropriate consideration been given by the applicant to the use of non-sentient alternatives? Is this clear on the application?

(ii) Choice of species.

(iii) Choice of method. What is to be examined, measured, recorded and is it appropriate to meet the objectives specified?

(iv) Number of animals.

(a) Scale of project.

(b) Statistical considerations: group sizes, number of groups. Are these appropriate to the power or precision required by the experiments or bioassays? Is the use of control groups appropriate? Minimise suffering whilst maximising information.

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

Cost of Animals

7. Most research programmes involve a range of species and procedures and it is therefore necessary to distinguish between the costs to different groups of animals submitted to different protocols. Thus, for each scientific protocol the scientist must submit:

(i) A sequential consideration of the use of each group of animals from the start to the end of their use, giving details of any combination or repetition of techniques, duration of restraint etc.

(ii) An assessment of possible adverse effects arising from the use set out at (i) above.

(iii) An account of the strategies to be adopted to avoid, minimise or terminate adverse effects (anaesthesia, analgesia, supervision, early killing etc).

8. With this information, a judgement can be made on the severity associated with the protocol in question. This is essentially a subjective judgement but it has proved possible to allocate a severity limit (mild, moderate or substantial) based on

the anticipated "worst case" scenario. This will represent the upper level of severity permissible for the procedure concerned. Procedures conducted wholly under general anaesthesia without recovery are not accorded a severity limit but are designated "unclassified".

9. It is then necessary to bring together the various assessments of severity and animal numbers from the individual protocols to arrive at an overall assessment of the severity of the entire programme of work. This process is set out in paragraphs 4.6 to 4.16 of the Home Office Guidance on the Operation of the 1986 Act.

What is missing?

10. Excluded from the elements in the justification or cost/benefit analysis set out so far are:—

(i) Training, experience and competence of staff.

(ii) Husbandry and housing conditions of the animals.

These are excluded not because they are not relevant but because they should be addressed by other elements in the control system: (i) by the personal licence and (ii) by the certificate of designation. Thus, in assessing the cost/benefit of research proposals on project licence applications the inspector should be able to assume staff competence and optimal animal housing and care.

11. Almost none of the elements in the cost/benefit assessment lend themselves to strict quantification. What is required is a balanced, rational judgement on justification based upon the information gathered under the three headings covered in paragraphs 5, 6 and 7 above. A strength of the UK system is that those making this essentially subjective judgement for most applications have the mix of expertise required to make simultaneous assessments on clinical, welfare, scientific and ethical aspects of research proposals. Inspectors have the clinical experience and skills to make informed judgements concerning the likely severity of adverse effects, the scientific experience and skills to enable sensible questioning of scientific quality and they are well placed to take a balanced view of the ethical extremes promulgated by those strongly committed in the debate over laboratory animal use.

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 prepa-

ration, 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 Prosecution 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.

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