

**SIXTH REPORT OF
THE ANIMAL WELFARE
ADVISORY COMMITTEE**

February 2002

ANIMAL WELFARE ADVISORY COMMITTEE

Introduction

- 1) This is the sixth report of the Animal Welfare Advisory Committee (AWAC) established in July 1996. The terms of reference (Annex A) are those approved by the Ministry of Defence (MOD). The Committee reports to the MOD Chief Scientific Adviser, however, as an advisory non-departmental public body (NDPB) the Committee is an independent group of specialist advisers acting in the public interest. The Committee's findings are published in order to inform Parliament and the public. Its role can, therefore, be summarised as acting as "the eyes and ears of the public" on matters relating to animal experimentation carried out by the MOD.
- 2) Since the fifth report the Committee's previous remit, DERA, (the Defence Evaluation and Research Agency) has been part privatised. The section that includes the majority of animal experimentation has been retained by the MOD and has been renamed Dstl (Defence Science and Technology Laboratory). Animal research for defence purposes is carried out by Dstl Porton Down. The CHS (Centre for Human Services) Alverstoke has been privatised and the section carrying out animal experimentation has been incorporated into a private agency (QinetiQ). It has been agreed between MOD and QinetiQ that the work at Alverstoke should remain within the Committee's remit.
- 3) During the course of this year, the Terms of Reference of the Committee were changed to reflect the new structure of animal use in defence research.
- 4) The fifth report was submitted in November 2000. The sixth report covers the period from 31st October 2000 to 28th February 2002. This longer interval is to allow the reporting year to be more closely matched to the annual returns of their animal numbers made by Dstl and QinetiQ to the Home Office. In the future, these will be used as a basis to start the AWAC reporting year. It is the intention of the Committee that future reports will be made every 12 months. This report is being circulated to a list of interested individuals and organisations as well as being placed in the library of the House of Commons and House of Lords. It is also available at the MOD website at <http://www.mod.uk>.

Use of animals by CBS Dstl and QinetiQ

- 5) Dstl uses animals in the fulfilment of its role to provide protective measures for the UK and its Armed Forces against the threat of chemical or biological weapons. In addition, research with animals is being carried out into the development of blast and ballistic protection, wound management and the biological effects of non-ionising radiation.

- 6) QinetiQ uses goats in simulated dives (using a dry pressure chamber) to allow them to establish safe escape strategies and to provide advice for submariners on escape procedures from crippled underwater vessels. Animals continue to be used because of the many variables that are investigated (pressure profiles, escape depth and gas mixtures). For example, if a crippled submarine is intact, it may be safe for the submariners to escape. However, if the hull is breached so that the submariners experience a period of increased pressure, the depth at which it is safe to attempt an escape is currently unpredictable.
- 7) The following points have been made in previous reports but merit repetition. There is continuing public concern over the use of animals in scientific research - in particular, defence research. Having made specific enquiries in previous years, the Committee can give an assurance that animals used in defence research programmes in the UK are regulated under the Animals (Scientific Procedures) Act 1986. No special exemptions apply. Animals used in Dstl establishments are subject to the same Home Office regulation and inspection as applies elsewhere. Dstl policy is to allow the AWAC Committee access to all animal facilities and to inform it of the types of work being undertaken. In accordance with the Committee's terms of reference, the Committee does not monitor compliance with the 1986 Act - that is the role of the Home Office Inspector.
- 8) The Committee, as in previous years, has consulted, inspected and made enquiries into all aspects of animal care and use in Dstl Porton and QinetiQ at Alverstoke. The Committee fully understands that publication of this report is subject to the constraints of national security and there is no intention of compromising the personal security of individuals in Dstl or QinetiQ establishments.

Meetings and operation of the Committee

- 9) It was hoped that replacements for retiring members of the Committee could be appointed early in the year but, unfortunately, it was not possible to appoint new members until October 2001. The Committee therefore delayed making any full site visits until the new members were in place, as these visits would contribute to their induction. Despite this delay, the Committee has met on five occasions during the reporting period. Two site visits have been made to Dstl Porton (12/10/01 and 15/2/02) and one to QinetiQ (14/1/02); this latter also included an internal Ethical Review Process review. The Committee has visited a laboratory animal breeder, to inform themselves on new husbandry techniques. The Committee has also held a management meeting at the Headquarters of the Royal College of Veterinary Surgeons (6/11/00). Individual members of the Committee have attended two training days at DERA (now Dstl). The first being part of a primate training course 22/1/01 and the second, a Personal Licence Holders Seminar on 'Modern Advances on Anaesthetics and Analgesia for Laboratory Animals' (29/3/01).
- 10) The Committee's full visits usually comprise a briefing from staff on recent activities and management structures, and visits to the animal accommodation and laboratories. In some instances, the Committee has been present during the carrying out of licensed

procedures, such as the simulated dives at Alverstoke. However, as stated above, it is important to understand that the Committee does not have a regulatory function and is not involved in a programme of inspection to ensure compliance with UK or European legislation. The Committee's role is to provide advice on welfare matters to the Chief Scientific Adviser (MOD). In addition, the Committee provides advice and feedback to management, scientists and animal care staff during site visits.

- 11) The 3Rs principles (that is, to adopt wherever possible measures for the Reduction of animal numbers in experiments, Refinement of procedures and husbandry, and Replacement with non-animal alternatives) were first formulated by Russell and Burch (1959). The 3Rs are now well accepted as a framework to improve laboratory animal welfare, and the Committee uses the principles as a basis for its enquiries at the Dstl and QinetiQ establishments.

Matters raised by the public

- 12) In its fifth report, the Committee noted some criticisms made by an anti-vivisection society relating to a paper published in the open scientific literature on the effects of sarin on marmosets by DERA employees. The Committee raised with Dstl the concerns made by the anti-vivisection organisation, specifically that: the experiments were unnecessary as sarin has been tested on animals; species differences are known; and human data are available. The Committee's terms of reference do not permit it to assess the justification for any specific study but it can report here that: the study was subject to DERA's ERP process and that the justification for the study in question was that it was aimed at determining whether low doses of sarin had a biologically important effect. The experiment had practical implications not only for battlefield situations but also for the debate concerning the long-term health implications of exposure to organophosphates. Moreover, the techniques used included a number of significant refinements of technique in order to minimise suffering, including home-cage behavioural testing (using touch screens with a reward system placed in front of the cage) and remote monitoring.

Numbers of procedures on animals carried out during the year 2000 at DERA establishments

- 13) The Committee receives an annual report from Dstl and QinetiQ on the numbers of procedures carried out on animals and the numbers of animals used for the first time. The statistics on the numbers of procedures carried out in the year 2000 are provided in the table below along with those of the previous five years. All of the procedures reported by Dstl, were carried out on animals used for the first time, so that the number of procedures equals the numbers of animals used for the first time. In the year 2000 61 goats were used in procedures for the first time at CHS/QinetiQ.

	1995	1996	1997	1998	1999	2000
Goat (Dstl)*			2	22	0	0
Goat (QinetiQ)**	153	124	127	124	149	80
Guinea pig	495	792	1,109	1,039	636	587
Hamster	0	42	396	222	144	24
Macaque	0	4	16	17	8	2
Marmoset	17	10	14	111	52	32
Mouse	6,706	7,701	8,569	7,477	10,144	10,856
Pig	48	48	85	96	84	106
Rabbit	39	19	31	48	10	19
Rat	1,406	2,428	717	1,999	410	350
Sheep	36	53	17	30	13	9
Ferret	0	0	0	30	0	0
Total	8,900	11,221	11,083	11,215	11,650	12,065

*Dstl – Defence Science and Technology Laboratory, Porton

**QinetiQ (previously CHS – Alverstoke (N.B. Goats are the only species used at QinetiQ)

Reasons provided by Dstl and QinetiQ for use of animals

14) The number of procedures returned to the Home Office by CBS for 2000 showed an increase of 484 (4%) over the 1999 figure to give a total of 11,985. The majority (91%) of the procedures were undertaken on mice. While the number of procedures on mice, pigs and rabbits increased, there was a reduction in the numbers of the five other species used. The fluctuation between years in the numbers of the various species used reflects changes in the research programme, dictated principally by MOD customers and the progression of programmes.

- 15) Mice. The mouse continues to be the most commonly used species and there was an increase of 7% in the number of procedures reported in 2000 to give a total of 10,856. The main emphasis of the work continues to be in the microbiological field including studies to gain a better understanding of disease progression and the development of vaccines and treatments for microbial and viral infections. The vaccine development programme continues to investigate alternative routes of administration e.g. oral and nasal. As the vaccine programme progresses toward clinical trials, the numbers of mice involved in each trial increase, in order to offer the statistical power necessary for regulatory studies. Similarly, whereas previous work with antibiotics has focussed on fully characterised therapeutics which are supported by a substantial body of clinical experience, the work has now turned increasingly toward more experimental, less well-characterised drugs. In such cases, pharmacodynamic studies (i.e. studies to determine key properties such as drug clearance time) have added substantially to the numbers of mice used, as have time-based studies of efficacy.
- 16) Rats. The use of rats decreased during 2000 to a total of 350 procedures, a reduction of 15% on last year's figures. The majority of the animals were used in one of two research programmes. One to investigate military concerns about the effects of radio-frequency radiation on brain electrical activity and the other to develop protective measures against chemically induced lung injury. Some animals were also used to investigate novel therapeutic approaches to protect against poisoning with chemical warfare agents. A small number of animals were used under terminal anaesthesia to investigate primary blast injury to the brain.
- 17) Guinea pigs. Guinea pig usage decreased by 8% to give a total of 587 procedures reported. The majority of the animals were used to assess the toxicity of compounds under investigation in the current programmes; most of the remainder were used in programmes to improve medical countermeasures against nerve agent poisoning. The guinea pig continues to be the best non-primate model for such areas of work. A small number of guinea pigs were used within programmes in the microbiological field to investigate the pathogenesis and treatment of virus infections.
- 18) Hamsters. The use of hamsters decreased significantly during 2000 to a total of 24 procedures, an 83% reduction on the previous year's figures. This decline is due to a move away from hamsters as models of some infectious diseases and towards the use of mice. However, they continue to be a valuable model for investigating prophylaxis and treatment of certain microbial infections.
- 19) Rabbits. A total of 19 procedures using rabbits were reported during 2000. All the animals were used in the microbiological field; just under half were used in the detection and identification of biological agents, and the remainder were used in programmes studying the immune response to microbial agents.
- 20) Pigs. The number of pigs used in licensed procedures increased from 84 to 106 and the majority were used in non-recovery (terminal anaesthesia) studies. Most of the pigs have been used in studies to develop personal protective equipment to protect against blast injury to the thorax. This work follows extensive studies using a

physical model of the thoracic wall that allowed evaluation of many armour designs. The result has been the development of a personal armour system, currently under manufacture, to protect personnel from thoracic blast injury. These studies have also allowed scientific investigations into optimal methods for the diagnosis and management of blast casualties.

- 21) Pigs were also used in studies to assess the efficacy of barrier creams against chemical challenge to the skin and the evaluation of novel treatments for chemically induced lung damage. The latter study represents a transition from a rodent model and has consequently reduced total animal usage. Studies evaluating new protective creams against skin damaging agents used 14 pigs. These experiments involved the animals being returned to the home pen for non-invasive, biophysical analysis for periods of up to six weeks. This technique has positive implications for the reduction and refinement of pig experiments in current skin research. In addition, skin harvested from non-recovery procedures was used for further validation of an *in vitro* skin system for the evaluation of medical countermeasures against chemical agents.
- 22) Sheep. Sheep have been used in a preliminary study evaluating the potential for low voltage electrical currents to prevent infection around orthopaedic implants. The results will serve as the basis for future research into new methods to control infection that do not rely upon traditional medicines such as antibiotics.
- 23) Non-human primates. The total number of procedures using non-human primates reported in 2000 was 34, a decrease of 43% from the previous year. Four marmosets and two macaques were used to provide blood samples. The remainder of the procedures were carried out on marmosets which were used to investigate the effects of the organophosphate sheep dip, diazinon, on primate behaviour and electrophysiology. This work was funded by DEFRA. Marmosets were also used to establish dose levels for a range of vaccines and pyridostigmine bromide (a pre-treatment used to protect against nerve agent poisoning) in preparation for a more sophisticated, longer-term study.
- 24) Goats. No goats were used at CBS in 2000. However, goats continue to be used at QinetiQ, Alverstoke to investigate the effects of decompression after a simulated dive, and to develop safe escape protocols and treatments for submariners trapped in disabled submarines. 80 procedures on goats were carried out in 2000, a reduction of 46% on the previous year. The reason for the decrease was a natural break in the research. The data already obtained from the animals have been used to inform a research program using human volunteers.

- 25) Ferrets. No procedures were reported for 2000.

External Peer Review

- 26) The Committee has been concerned that defence research using animals should be published, where possible, in peer-reviewed open journals. This is to ensure that the research carried out is of high quality. The Committee is, therefore pleased to have

had sight of a list of 115 peer-reviewed unclassified publications from Dstl. Of these, approximately 50% either directly involved the use of animals, were underpinned by the use of animals or addressed alternatives to animal use.

- 27) QinetiQ carries out collaborative research with a number of other institutions and has published five papers involving the use of animals in open peer-reviewed journals.

LD₅₀ tests and their use at Dstl

- 28) In last year's report we described the changes that have taken place with respect to the LD₅₀ test. Specifically that LD₅₀ tests are currently being superseded by more humane techniques in civilian regulatory toxicity.
- 29) Dstl continues to occasionally seek permission from the Home Office to carry out LD₅₀ tests. The Committee has sought further clarification from Dstl for their continuing need for this test, and has received another briefing on this subject.
- 30) There remains a fundamental difference between the requirements of a research programme aimed at defending military personnel, where it is necessary to determine the killing dose of extremely toxic chemicals, compared to the more modest requirements of regulatory toxicity. Regulatory toxicity requires an understanding of the minimum dose likely to produce adverse effects and the relationship of this higher dose to the lower therapeutic dose of the medicine. Dstl requires a thorough understanding of the toxicity of potential chemical and biological agents, and may also need information on the biological impact of exposure over a wide range of doses.
- 31) Dstl's position regarding obtaining permission from the Home Office to carry out these tests is no different to that of any other research organisation. In each case, Dstl has to specifically justify the need to carry out a LD₅₀ to the Home Office and the application is subjected to the normal cost/benefit analysis.

Animal facilities

- 32) The Committee has visited the experimental animal house, the large animal unit and the external facilities of the animal breeding unit at Dstl. It has also visited the goat accommodation at QinetiQ, including paddocks and quarantine facilities, and seen the pressure vessel used to simulate escapes from a submarine. The Committee felt that the accommodation and care was generally satisfactory. It was clear that efforts are made to meet the needs of the different species. During such visits, the Committee takes the opportunity to provide individual comments on the accommodation and to make suggestions for improvements. These are not necessarily criticisms of existing facilities but are offered in the hope of leading to ever better housing. For example, in this reporting year, the Committee has asked that advice be sought from large-animal experts on ways of improving the social housing of pigs in short-term accommodation.

33) The accommodation for goats at Alverstoke is old. The Committee was, therefore pleased to be informed that there are plans to develop new improved accommodation and will follow the development and implementation of these plans with interest.

3Rs audit trail

34) The Committee has previously commented on the desirability of introducing a 3Rs audit trail. The benefits of such a trail are that it focuses the attention of staff on the continuing need to address the 3Rs. It also reminds them of the need to publish advances either with research papers or separately. The Committee was pleased to receive from Dstl a document containing the following examples:

- The introduction of non-invasive biophysical measurement techniques in studies aimed at assessing the effectiveness of therapies against vesicating agents. These techniques include the use of skin photometry to replace serial killings of animals to obtain samples for histological analyses. Other probes have been developed to measure water loss through the skin. A further refinement of measurement techniques has been training the pigs to respond to simple verbal/visual commands so that these biological measurements can be obtained in the home pen environment without the need for sedation or anaesthesia.
- The development of a model using nematode worms to screen attenuated bacterial mutants. Such a model could lead to a substantial decrease in the numbers of rodents needed in future studies. This work has been supported by a combination of Animal Procedures Committee and MOD funds.
- Following the Committee's promotion of the animal welfare benefits of animal training, Dstl have made significant advances in training non-human primates to co-operate in studies. The Committee has been shown a novel system, which precludes the need for restraint during performance of a visual task.
- Dstl continues to develop and promote the application of remote monitoring devices. Although use of some of these does require a surgical procedure, they can subsequently allow the animals to be studied in their home cage with their cage-mates, reducing or eliminating the need for capture or restraint. Dstl is also developing the use of devices that are attached externally (e.g. to collars) and that do not require a surgical procedure.
- A programme of environmental enrichment has been developed and introduced for mice held under high levels of biocontainment.
- The Committee is pleased to note that Dstl makes considerable efforts both to learn about and to communicate new advances in the 3Rs. For example, Dstl holds a number of workshops, seminars and training days, some of which have been attended by members of the Committee. The Committee noted that the training day seminar attended was impressive in that the speaker was a world-wide expert in his field and that questions by staff were encouraged. We are also

pleased to note that a paper outlining the methods used at Porton to advance the 3Rs has been published in the Journal of Defence Science. Over the past year, in-house specialist working groups have been established in both small-animal and non-human primate user communities to promulgate and disseminate best practice. These are reported to have resulted in an increased awareness of welfare issues and modification of procedures.

35) The Committee has seen some of these innovations during its visits and will encourage and explore further developments in the coming year.

36) There have been perceived benefits at both Dstl and QinetiQ as a result of the introduction of the Ethical Review process which has been used since 1995. (The Ethical Review Process became a Government requirement in 1999). These include closer and wider scrutiny of license applications, increased communication between staff on animal welfare issues, and a greater authority given to animal care staff.

37) The Committee will continue to request an annual 3Rs audit.

Future activities

In the coming year the Committee, under the chairmanship of Mr Brian Hoskin, will continue its induction of new members. It will also continue to follow up current lines of enquiry, including:

- Numbers of animals bred and used and the reasons for their use
- Animal care and husbandry including monitoring of the building programme
- Training of animals
- 3Rs audit
- Monitoring and facilitating the development of the ERP

Dr Robert Hubrecht (Chairman)
Dr Jeremy Lucke (until October 2001)
Canon Dr Maureen Palmer
Dr Tim Morris (from October 2001)
Mr Brian Hoskin (from October 2001)
Dr Peter Thornton (from October 2001)

Contact point:

*AWAC Secretary
Dstl Corporate Affairs
Room 26, Bldg A1
Dstl Fort Halstead
Sevenoaks, Kent, TN14 7BP*

ANIMAL WELFARE ADVISORY COMMITTEE

TERMS OF REFERENCE

General

1. The Animal Welfare Advisory Committee (AWAC) is an independent Non-Departmental Advisory Body. The Committee will review the care and welfare arrangements for animals used in procedures for defence research purposes in the UK.

Conditions

2. The Committee is appointed by the Ministry of Defence's Chief Scientific Adviser (CSA) and will report to him at least once each year. The reports will give independent advice and all unclassified information will be published.

Specific Guidance

3. The Committee will review:
 - 3.1 The operation and effectiveness of the Animal Care and Use Committees;
 - 3.2 The operation and effectiveness of the Ethical Review Process for projected scientific work involving the use of animals;
 - 3.3 Implementation and the audit of the 3 Rs principle; Reduction, Refinement and Replacement (as defined by W M S Russell and R L Burch in 'The Principles of Humane Experimental Technique 1959' Methuen and Co London;
 - 3.4 External peer review of the results of scientific work involving animals;
 - 3.5 Broad trends in the numbers of animals used and the numbers of animals bred under the Animals (Scientific Procedures) Act annually;
 - 3.6 Local control over any procedures on live animals not covered by the Animals (Scientific Procedures) Act, e.g euthanasia;

- 3.7 Training and education programmes for all relevant personnel on the use and care of animals;
- 3.8 Initiatives to ensure the maintenance of high standards of animal welfare in defence research establishments.

The Committee is not responsible for monitoring compliance with the Animals (Scientific Procedures) Act. This is the duty of the Home Office.

Composition

- 4. Appointments to the AWAC will be by the authority of the CSA, MOD. There will normally be four members of the Committee including the appointed chairman. Members would be expected to serve for a period of 3 years but a second term may be allowed with the agreement of both CSA and the Committee. The secretariat will be provided by Dstl.