NC3Rs

National Centre for the Replacement, Refinement
and Reduction of Animals in Research

Foundations for success

Annual Report 2005

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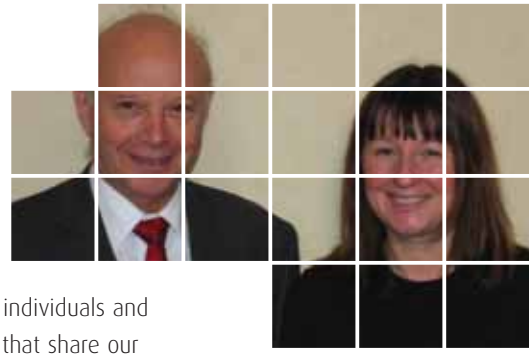


Foreword

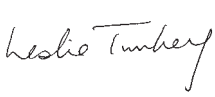
The inaugural year of the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) has been an exciting and productive one which has seen the development of a broad and ambitious work plan, increase in funding from the public, charitable and private sectors and the fostering of collaborations. The Centre has developed a work plan which encompasses all of the 3Rs and balances the investment in new knowledge and technologies through research awards with improving access to, and implementation of, existing information.

Increasing the investment in research, where the primary objective is to advance knowledge in the 3Rs, is pivotal to our success. We have been delighted to award eight research grants in 2005 totalling almost £1 million and our aim is to build on this investment in future years. While providing funds for research is important, we also recognise that much can be achieved by investing relatively small amounts in pilot studies, exchange visits and training. With this in mind we have been pleased to forge an important partnership with the Laboratory Animal Science Association (LASA) to provide awards of up to £2k each and our joint initiative has awarded 14 grants in 2005, encompassing all of the 3Rs and, importantly, providing a valuable resource for animal care staff.

Providing easy access to information on the 3Rs is high on the Centre's priorities. In September, we launched our website - a comprehensive and interactive resource on the 3Rs with information for all of our stakeholders. Feedback on the website has been overwhelmingly positive.

Working with individuals and organisations that share our commitment to and philosophy on the 3Rs has been an important part of our success this year. We are keen to maximise our impact by sharing expertise, experience and resources and to avoid duplication.

We have been enormously encouraged by the support that our efforts have attracted from all of our stakeholders and in particular the scientific community and industry, since it is here that there is the most opportunity to achieve our objectives. The challenge will be to build on this momentum for 2006.

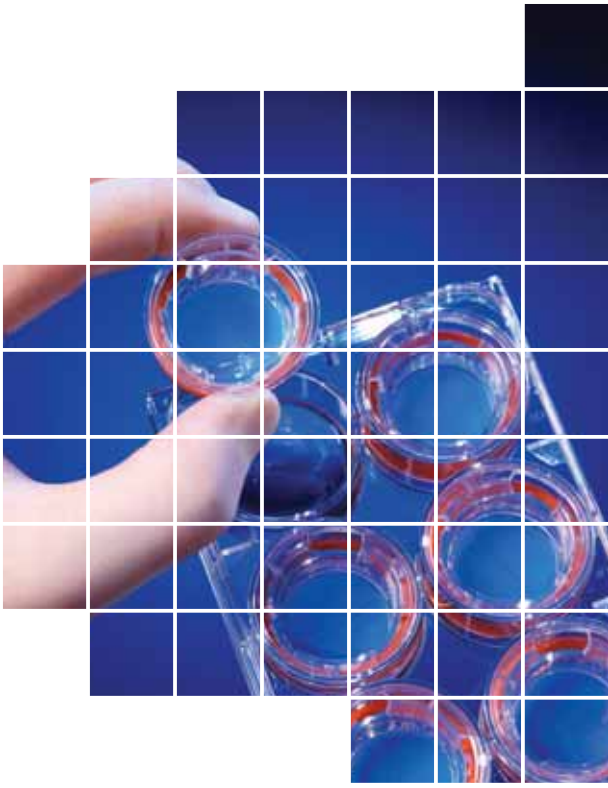


Leslie Turnberg
Chairman

Vicky Robinson
Chief Executive

Summary of key successes

- Involvement of all stakeholder groups in the development of a broad programme of initiatives covering all 3Rs
- Increased and new funding from Government, industry and charities
- Investment of £1.5 million in research grants since launch
- Launch of a new comprehensive and contemporary website
- Forging of new partnerships and collaborative activities



Launch of the NC3Rs

In September 2004, the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) was launched by the Parliamentary Under Secretary of State for Science and Innovation, Lord Sainsbury, as a UK focus and catalyst for the development and implementation of the 3Rs - the ethical principles which underpin the humane use of animals in scientific research and testing. The establishment of the NC3Rs implemented the 2002 recommendation for a national 3Rs centre made by the House of Lords Select Committee on the Use of Animals in Scientific Procedures.

Bringing together stakeholders in academia, industry, Government, regulatory authorities and animal welfare and protection groups, the NC3Rs is a scientific organisation which aims to advance the 3Rs by funding laboratory research, raising awareness, improving access to information and fostering collaborations which bring together expertise and resources. A non-executive Board, chaired by Lord Turnberg of Cheadle, has been appointed to advise on and approve the NC3Rs strategy and work plan. Members of the Board have expertise in all aspects of the 3Rs. Delivery of the Centre's work plan is through an expert scientific and administrative team, lead by the NC3Rs Chief Executive, Dr Vicky Robinson.

At its launch, the NC3Rs had a total annual budget of £696k from the Department of Trade and Industry (from the Medical Research Council (MRC) and Biotechnology and Biological Sciences Research Council (BBSRC)) and the Home Office. During 2005 significant additional funding has been secured from the Government, the Wellcome Trust and the Association of the British Pharmaceutical Industry (ABPI).

The 3Rs

The principles of the 3Rs - Replacement, Refinement and Reduction - were clearly articulated by UFAW Scholars, William MS Russell and Rex L Burch and published in 1959 in their book *The Principles of Humane Experimental Technique*. The 3Rs are now enshrined in national and international legislation regulating the use of animals in scientific procedures, including the UK Animals (Scientific Procedures) Act 1986.

Replacement
Methods which replace or avoid the use of animals.

Refinement
Methods of husbandry and procedures which minimise actual or potential pain, suffering or distress, or enhance animal welfare.

Reduction
Methods which enable researchers to obtain comparable levels of information from fewer animals, or to obtain more information from the same number of animals.

Board Membership

Lord Turnberg of Cheadle (Chair)

Professor Paul Flecknell - University of Newcastle (Deputy Chair)
Anaesthesia, analgesia, refinement

Dr Vicky Robinson - NC3Rs
3Rs, welfare of genetically altered mice

Professor John Bell - University of Oxford
Medicine, immunology, genetics, genomics

Dr Diana Dunstan - MRC
Research funding

Dr Julia Fentem - Unilever
Chemicals risk assessment, new (replacement alternative) testing approaches

Dr Michael Festing - University of Leicester
Genetics, experimental design and statistics

Dr Lesley Heppell - BBSRC
Research funding

Dr Bryan Howard - LASA
Refinement, antibody production, veterinary science

Professor Jane Hurst - University of Liverpool
Animal behaviour and welfare

Dr Maggy Jennings - Royal Society for the Prevention of Cruelty to Animals
Animal welfare, ethics, training, refinement

Dr James Kirkwood - Universities Federation for Animal Welfare
Veterinary science, animal welfare

Dr Jon Richmond - Animals (Scientific Procedures) Division, Home Office
Regulation, trends in animal use

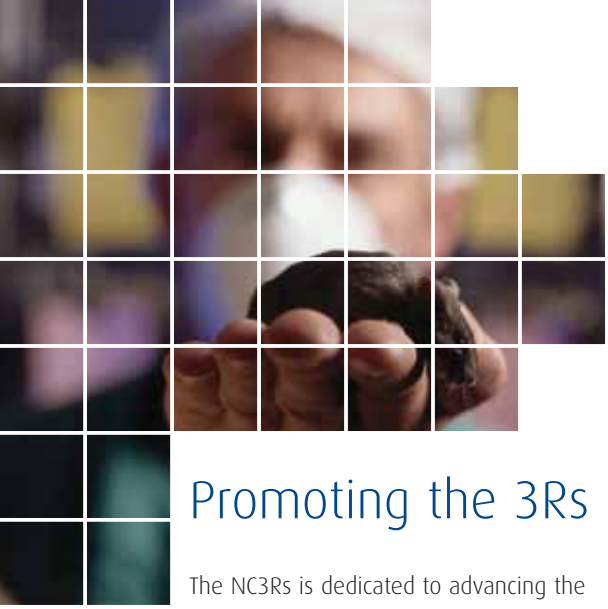
Professor Nancy Rothwell, DBE - University of Manchester
General physiology, brain disease, neuroimmune interactions

Professor Malcolm Rowland - University of Manchester
Physiological modelling and prediction, pharmacokinetics, drug development

Dr David Smith - AstraZeneca
Pharmaceutical research, regulatory toxicology, non-rodents, reduction

NC3Rs focus

The NC3Rs has a broad range of stakeholders including scientists and animal care staff in academia and industry, regulatory authorities, Government, animal welfare and protection groups, the public and the media. The primary focus of its activities is the scientific community and those actively involved in research as this is where there is the greatest opportunity to influence the development and implementation of the 3Rs.
The NC3Rs also provides authoritative and balanced information on the use of animals and the 3Rs for non-specialist audiences.



Promoting the 3Rs - strategy in action

The NC3Rs is dedicated to advancing the implementation of the 3Rs. The replacement of animals in research and testing is the ultimate goal of the NC3Rs. The Centre recognises, however, that there are significant and complex scientific, technological and regulatory hurdles to overcome, which make replacement in some areas a long-term objective. Thus, while the use of animals continues to be necessary, the NC3Rs is committed to developing initiatives which minimise the numbers used and improve animal welfare. The NC3Rs strategy therefore provides for a balanced portfolio across all of the 3Rs.

All stakeholder groups have been included in the development of the NC3Rs strategy and delivery of its work plan (e.g. through membership of its working groups and panels etc). In January 2005, the Centre hosted the first of its annual one-day stakeholder meetings. Attended by over sixty participants from academia, industry, regulatory authorities, research funders, and animal welfare and protection organisations, the meeting provided a platform to consider priorities and opportunities for working together, which the NC3Rs has subsequently built upon. There is general consensus amongst all stakeholder groups that the NC3Rs should prioritise its activities into three broad categories - funding 3Rs research; raising awareness on what can be done to implement the 3Rs; and providing better access to information and resources to facilitate this, including through collaborations and partnerships. This has been translated into the NC3Rs work plan for 2005.

Research grants awarded in 2005

Cell lines for prediction of drug metabolism and toxicity in man

Professor Wolf, CXR Biosciences Ltd - £181k

Pharmaceutical and consumer product companies are required by law to test their products for potential toxic effects before marketing them. In many cases, testing in animals remains the most reliable predictor of toxicity in the human. Toxic effects in animals are not always directly representative of toxicity in a human, however, and the development of humane alternatives, which reliably predict human toxicity and are economically viable, is desirable. One possible alternative is the use of human cells or tissues in culture. Human tissues, however, are not available in the quantities necessary for routine testing purposes on an industrial scale, and immortalised human cell lines that can be grown continuously in culture do not reproduce the characteristics of whole organs, such as the liver, where toxic effects are most often seen. The aim of this project is to genetically modify existing animal cell lines to express human cytochrome P450, which is primarily responsible for drug metabolism in the liver. By humanising cell lines which also have reporter genes to allow simultaneous detection of toxic effects such as oxidative stress, DNA damage, apoptosis or cell cycle arrest, or hyperplasia the possibility of using these cells to reliably and rapidly predict toxic effects in humans will be investigated, thus potentially replacing the use of animals.

Funding high-quality 3Rs research

Traditionally there has been little funding specifically allocated for 3Rs research and many advances have arisen as an indirect output of other research programmes. Some funding bodies support basic research relevant to the 3Rs, however, in 2005, the NC3Rs launched a response mode funding scheme to support high-quality basic and applied research. This successful scheme is continuing to increase investment in 3Rs research, advance knowledge, improve methodologies and technologies and facilitate novel and multidisciplinary approaches.

Forty applications for funding were received. All applications were peer reviewed by national and international referees and assessed and ranked by an expert panel according to the scientific quality and potential impact on the 3Rs. Eight grants, totalling almost £1 million, were awarded. This 20% success rate is consistent with the UK Research Councils and major research charities.

Research grants awarded in 2004

Dr Roughan, University of Newcastle - £212k
Neoplasia and pain in laboratory animals

Professor Bibby, University of Bradford - £175k
A novel approach to the preclinical assessment of novel anti-cancer agents

Professor Nicol, University of Bristol - £136k
Behaviour as an indicator of welfare state in genetically modified mice

The grants awarded covered all aspects of medical, biological and veterinary research. Six of the grants focussed on the replacement of animal use, one on refinement and one on reduction.

Research grants awarded in 2005

Professor Wolf, CXR Biosciences Ltd - £181k
Cell lines for prediction of drug metabolism and toxicity in man

Professor Thomas, Cardiff University - £235k
The development of a cell-based diabetic wound bioassay

Dr Turrell, Fisheries Research Services - £128k
Replacement of the mouse bioassay: development of SPE and LC-MS for detection of paralytic shellfish poisoning toxins

Dr Smith, University of Sheffield - £100k
Reduction in animal usage by multiple antigen immunisation schedules

Professor Ward, Keele University - £43k
Maintenance of *Lutzomyia longipalpis* colonies using an artificial membrane blood-feeding method

Dr Tucker, University of Cambridge - £153k
Development of an air-interface *in vitro* organ culture (IVOC) of bovine respiratory epithelium

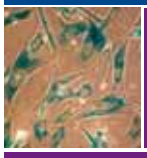
Dr Redhead, Invervet UK Ltd - £112k
Development of replacement *in vitro* assays for the quantification of clostridial vaccine antigens

Professor Lemon, University College London - £17k
Development of a new tissue-friendly head implant for use in brain studies in monkeys

Raising awareness and disseminating information

Sourcing information on the 3Rs and best practice can be problematic, either because it is not published or widely disseminated or because it is not easily identified. Improving access to high-quality information on the 3Rs is a key function of the NC3Rs. To complement this, the NC3Rs also collates and reviews information on the 3Rs, synthesises best practice guidelines and identifies gaps in knowledge. In 2005 a number of initiatives were developed to raise awareness and facilitate implementation of the 3Rs.

Research grants awarded in 2005



The development of a cell-based diabetic wound bioassay

Professor Thomas, Cardiff University - £235k

Impaired skin wound healing affects up to 15% of people with diabetes. Currently, no suitable model exists for the study of diabetic wound healing and studies in animals involve painful procedures. This project aims to develop a simple, reproducible, *in vitro* diabetic wound model system by characterising fibroblasts from leg ulcers from diabetic patients and comparing them to fibroblasts from non-diabetic patients. Normal and diabetic fibroblast cells will be used to create stable cell lines and by comparing their patterns of gene expression, biomarkers of diabetic wound disease will be identified and used to develop a cell-based reporter system, thus potentially replacing animals. This will lead to the automated testing and pre-screening of reagents that may help in the treatment of skin wounds due to diabetes.

Website - the UK's first comprehensive 3Rs resource

In September 2005, the NC3Rs launched its website (www.nc3rs.org.uk) - an interactive, comprehensive and contemporary resource on the 3Rs. The website is the Centre's main interface with its stakeholders, providing detailed information on the NC3Rs mission, strategy, work plan and funding schemes. The site also has an Information Portal which is a gateway to high-quality information on the 3Rs, covering a broad range of topics from advice on searching databases for alternatives to the use of animals, to anaesthesia and analgesia. The Information Portal provides annotated links to online databases, websites, journal articles, legislation and other publications, selected by experts for their relevance, quality and utility. The website also aims to stimulate awareness and interest in the 3Rs through its commissioned articles on topical 3Rs issues written by experts and its Viewpoints section.

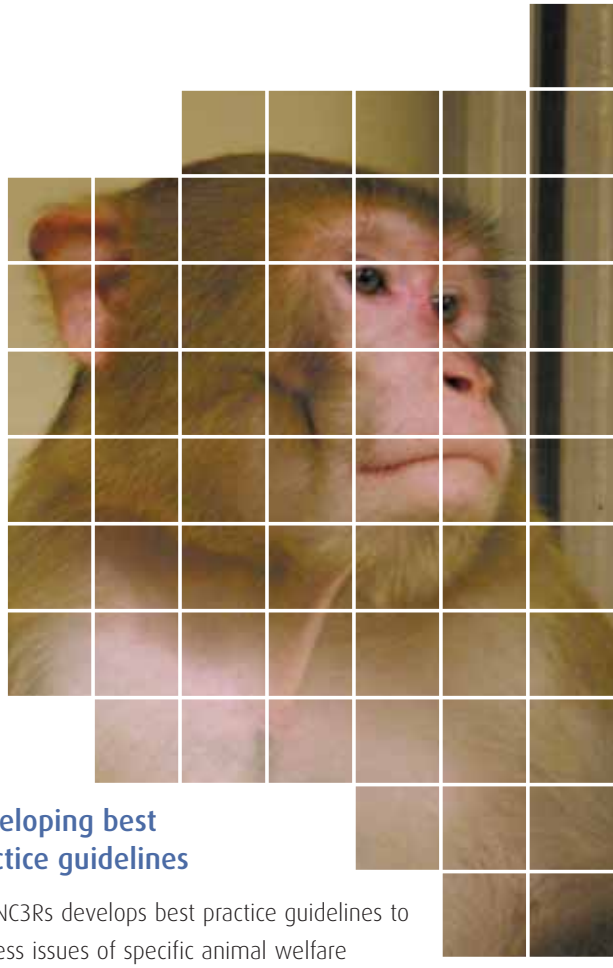
Research grants awarded in 2005

Replacement of the mouse bioassay: development of SPE and LC-MS for detection of paralytic shellfish poisoning toxins

Dr Turrell, Fisheries Research Services - £128k

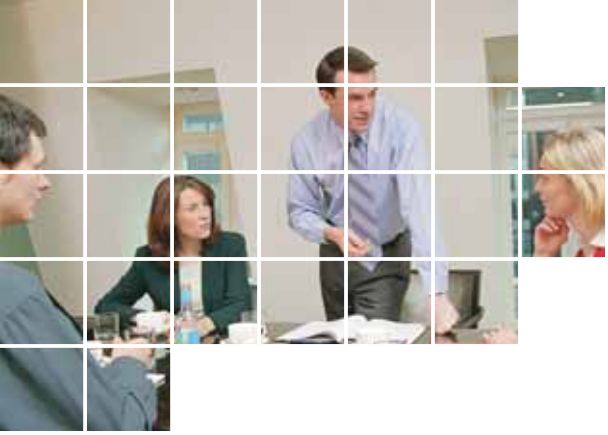
Bivalve molluscs such as mussels, oysters and scallops feed by filtering algae from the water. Some of these algae produce toxins, which are harmless to the shellfish, but toxic to organisms further up the food chain including humans. Globally, the most common shellfish poisoning syndrome caused by bioaccumulated toxins is paralytic shellfish poisoning (PSP). In the UK, levels of PSP toxins that exceed the legal limit are detected, and concentrations greater than those quoted as causing illness or death have been found.

In the European Union, legislation requires the monitoring of shellfish for the presence of these toxins. Currently, PSP toxins in shellfish are monitored using the AOAC mouse bioassay. This involves the extraction of shellfish meat in heated, acidified water followed by injection of a sample of the extract intraperitoneally into mice. The end point of the assay is the death of the injected mice, which indicates the presence of PSP toxins. The aim of this project is to develop and optimise an analytical test to replace the AOAC mouse bioassay, using solid phase extraction (SPE) with liquid chromatography and mass spectrometry (LC-MS) for the detection and quantification of PSP toxins in shellfish.



Developing best practice guidelines

The NC3Rs develops best practice guidelines to address issues of specific animal welfare concern. In 2005, the NC3Rs established an expert working group to identify refinements in the use of food and fluid management in macaques used in behavioural neurosciences research, where animals must perform various tasks (e.g. press a lever, touch a computer monitor, use a joystick) in order to obtain their daily fluid or food allowances. The working group will produce guidelines which detail refinements and current best practice and identify areas of research to substantiate the development of further refinements.



Exchanging information and ideas

Bringing researchers, animal care staff, veterinarians, regulators and others together through symposia and workshops to exchange views, expertise and experience provides a valuable platform for education and dissemination of the 3Rs. In 2005, the NC3Rs:

- Launched an annual free workshop on non-human primate[1] welfare. The inaugural meeting focussed on refining husbandry and procedures by training animals to cooperate through training and socialisation. Attracting over 75 participants, from 28 organisations, the workshop comprised talks from experts in the field and themed discussion on practical issues around the use of training as a refinement.
- Hosted a free symposium for animal care staff on improving the welfare of laboratory animals. Covering a diverse range of topics from socialising dogs to euthanasia of rodents, the symposium attracted 90 participants from 36 establishments in academia and industry. The symposium will be held annually.

Networking

Throughout 2005 NC3Rs staff have given presentations on the Centre, the 3Rs, and specific projects, at a wide range of scientific conferences, symposia and research organisations. As a result of this the Centre's influence and network has increased considerably. NC3Rs staff are active members of a wide range of external committees and working groups - analysing data, reviewing literature and writing scientific publications, guidelines and recommendations.

[1] Referred to herein as 'primate'

Research grants awarded in 2005

Reduction in animal usage by multiple antigen immunisation schedules

Dr Smith, University of Sheffield - £100k

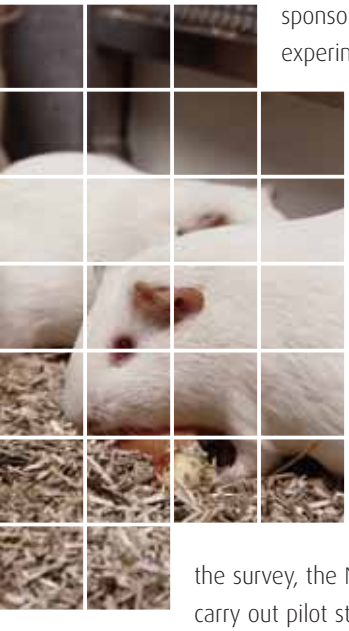
Polyclonal and monoclonal antibodies are used in clinical diagnosis, as therapeutic reagents and in academic research. The production of antibodies involves the use of animals, usually mice or rabbits. This project aims to reduce the number of animals used for antibody production by determining whether it is possible to extract different antibodies, each with the correct specificity, from animals vaccinated with more than one antigen (similar to a combined vaccine). Current immunization procedures involve injecting single antigens into one or more animals; two rabbits or five mice are often used for each antigen. If multiple antigens, injected simultaneously, could be shown to elicit the same specific response as that achieved with a single antigen, this could reduce by 50% the number of animals needed. For monoclonal antibody production, ease of screening means that it may be possible to use vaccines containing three or even four antigens for each animal, reducing the number of animals required by up to 75%.

Collaborations and partnerships

To maximise its resources, expertise and outreach, the NC3Rs has engaged a range of organisations in collaborative activities on key 3Rs issues.

Reducing the use of animals through improved experimental design

Anecdotal evidence suggests that not all research programmes involving the use of animals are exemplars of experimental design and statistical analysis and that there is, therefore, scope for improvement and the potential to minimise animal numbers. In collaboration with the US National Institutes of Health's Office of Laboratory Animal Welfare, the NC3Rs is sponsoring a detailed survey of the quality of experimental design and statistical analysis in published papers which use animals and which acknowledge funding from any UK or US public body. An expert working group has been established to oversee the study and a US and UK statistician have been appointed to undertake the review. In 2005, a pilot study was carried out in order to optimise the project plan and a full survey of 300 papers has now commenced. The results of this study will be used to guide future NC3Rs activities in this area. In addition to the survey, the NC3Rs is drafting guidance on how to carry out pilot studies and reviewing how information on animal care and use is reported in the methods section of scientific papers.



Research grants awarded in 2005

Maintenance of *Lutzomyia longipalpis* colonies using an artificial membrane blood-feeding method

Professor Ward, Keele University - £43k

The sand fly, *Lutzomyia longipalpis*, is of medical and veterinary importance as it transmits *Leishmania infantum*, the parasite that causes visceral leishmaniasis. Visceral leishmaniasis affects approximately 500,000 people worldwide each year, and is fatal if not treated.

Research into the parasite and its transmission often requires colonies of sand flies to be maintained within laboratories. Female sand flies require a blood meal to provide nutrition for egg production and in the laboratory this is commonly achieved by allowing the female flies to blood-feed on an anaesthetised hamster. Recent research has described alternative methods of artificial blood-feeding for other species of sand flies using chick-skin membranes and chicken or horse blood. The aim of this project is to determine the viability of these *in vitro* methods for maintaining a laboratory colony of *Lutzomyia longipalpis*.

3Rs Prize - raising the kudos of 3Rs research

There is increasing recognition within the scientific community that research which directly or indirectly advances the 3Rs is an important output - to ensure high-quality, reproducible and humane science, and to address public concerns about the use of animals.

Nevertheless, within some sectors, there is a need to raise the status of research in this area. To complement its funding scheme, in 2005 the NC3Rs launched a prize to recognise a piece of research, published in the previous 12 months, which makes a significant contribution to the 3Rs in medical, biological or veterinary research. The £10k prize, sponsored by GlaxoSmithKline, will be awarded to Dr Siouxsie Wiles (Imperial College London) at the NC3Rs annual stakeholder meeting early in 2006 for her work on refinement of a mouse model of bacterial transmission and infection.

Research grants awarded in 2005

Development of an air-interface *in vitro* organ culture (IVOC) of bovine respiratory epithelium

Dr Tucker, University of Cambridge - £153k

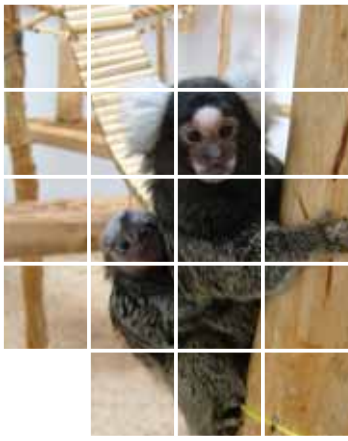
The bacterium *Mannheimia haemolytica* causes bovine pneumonic pasteurellosis (or shipping fever), a major respiratory disease in cattle. Bovine herpes virus (BHV-1) respiratory infections are also widespread in cattle. BHV-1 infection alone is not life-threatening but predisposes the cattle to secondary bacterial infections, which may result in death. Understanding the precise molecular mechanisms of these infections is critical for the development of effective strategies for the prevention and treatment of these diseases.

The aim of this project is to use organs from animals killed for food to establish and characterise a physiologically relevant, *in vitro* respiratory tract organ culture system that can be used to study the early stages of the pathogenesis of bovine bacterial and viral respiratory infections.

Supporting small scale 3Rs research projects

Funding is often required to carry out small scale research projects and for exchange visits or training in the 3Rs. Sources of such funding, particularly for veterinarians and animal care staff, are limited. To address this, the NC3Rs has launched a Small Awards Scheme, in collaboration with LASA. In 2005, 19 applications for funding were received and reviewed by an expert panel and the following awards were made:

1. Development of an *in vitro* methodology for renal toxicity
2. Animal technician exchange visits and training
3. Use of fMRI to identify brain regions involved in nociception in fish
4. Effects of airflow and substrate on ammonia levels in IVC mouse cages
5. Development of electronic teaching materials on refinements in primate husbandry and care
6. Further development of an *in vitro* model of the rat nasal cavity for screening of upper respiratory toxins
7. Determination of the welfare and housing requirements of axolotls



8. Use of *in vitro* model systems to quantify the potential use of optical biopsy in medical research
9. Musculo-skeletal modelling to reduce the need for invasive techniques in studies of animal biomechanics
10. Training and development in Intra-Cytoplasmic Sperm Injection as a method for reducing the number of animals used to maintain GM lines
11. Effects of capture, transportation and social reorganisation on health, survival and reproduction of rhesus macaques
12. Replacing the use of animal blood derivatives in experiments to test artificial joint materials
13. Replacement of the Mouse Antibody Production test with PCR - evaluation of the quality of DNA extracted from biological samples
14. Use of confocal microscopy as a refinement for the assessment of aberrant crypt foci and intestinal tumours in mice

Challenging primate use in drug discovery and development

The most common scientific use of primates in the UK is in the assessment of pharmaceutical safety and efficacy evaluation. The use of primates in regulatory toxicology has recently been reviewed by the Animal Procedures Committee, however there has yet to be a comprehensive scientific review of the rationale for this use and of 3Rs opportunities across all areas of use in drug discovery and development.

In 2005, in partnership with the ABPI, the NC3Rs has developed a strategy for reviewing and challenging the use of primates in drug discovery and development with the aim of minimising use and enhancing implementation of the 3Rs. Four areas - drug dependency, pharmacokinetics, regulatory toxicology and biologicals (e.g. antibodies, vaccines) have been identified as priorities for consideration. Under the umbrella of an expert steering group, four working groups have been established to consider primate use in these areas, focussing on scientific rationale for use and potential reduction and replacement strategies, regulatory pressure for use, obstacles to implementing the 3Rs and harmonisation and refinement of study designs.

Research grants awarded in 2005

Development of replacement *in vitro* assays for the quantification of clostridial vaccine antigens

Dr Redhead, Invervet UK Ltd - £112k

Clostridial bacteria produce toxins which cause a range of diseases in farm and companion animals. Veterinary vaccines against these diseases are often developed from the toxin itself. The toxins can be treated to destroy their toxic properties, leaving a harmless form (a toxoid), which, when used in a vaccine, is able to stimulate production of antibodies which will recognise the original clostridial toxin, thus protecting the vaccinated animal from disease.

During the manufacture of the vaccines the amounts of toxins and toxoids must be measured as a regulatory requirement, and to ensure consistent quality of the vaccines. Currently this involves the use of animals. The aim of this project is to replace the use of animals by developing and characterising *in vitro* assays based on the use of specific cell lines and antibodies to quantify the toxins and toxoids.

3Rs and the use of rodents in single dose acute toxicity studies

The NC3Rs coordinates a European initiative to challenge the use of rodents in single dose acute toxicity studies in pharmaceutical development. Involving eleven pharmaceutical companies and three contract research organisations, the initiative is in two phases.

The first phase involves harmonising the study design for acute toxicity studies, with emphasis on reducing the number of animals used and minimising suffering through early humane endpoints. This phase was completed in 2005. It demonstrated that data obtained from acute toxicity studies were not used for termination of a compound during drug development or to set the starting dose of a compound for clinical trials in man. Carrying out these studies later in the drug development process could, therefore, significantly reduce the number of animals used.

Currently, conventional single dose acute toxicity studies are the only study type in drug development where lethality is a defined endpoint. The aim of these studies is to identify the dose which causes major adverse effects and therefore provide data to predict overdose in man. The second phase of the initiative, which commenced in 2005, is to develop a strategy for challenging the guidelines which require conventional acute toxicity studies. Part of this process involves the comparison of data from preclinical studies of pharmaceutical drugs with available data from human overdoses, in partnership with the European Poisons Centre in Lyon.

Research grants awarded in 2005

Development of a new tissue-friendly head implant for use in brain studies in monkeys

Professor Lemon, University College London - £17k

In some studies of brain function using primates, where recordings are taken from single nerve cells in the brain, it is necessary to restrain the head of the monkey, usually by the insertion of an inert metal implant into the skull. Tissue around the implants can become infected and additional surgery may be required should devices become broken or loose. This project aims to refine the current methodologies to minimise suffering by using a three-dimensional reconstruction of the skull to guide the construction of a custom-fitted head-holding device, made from a tissue-friendly polymer.

Replacement the ultimate goal

Over 85% of the Centre's 2005 investment in research awards was for projects to replace the use of animals. To further support its commitment in this area the NC3Rs has established an expert advisory group to advise on further opportunities for replacement. The group, which has expertise in a range of replacement alternatives, including tissue engineering, vaccine development and *in vitro* technologies, will assist the NC3Rs in horizon scanning to identify and exploit new scientific and technological developments that may allow animals to be replaced in some areas of research and testing.

Financial summary

Auditor's statement

The NC3Rs accounting period runs from the beginning of April to the end of March each year.

Financial year April 04 - March 05

At its launch in May 2004, the NC3Rs had an annual budget of £696k as indicated in Figure 1. The work of the NC3Rs did not formally commence until September 2004 when its Board met for the first time and therefore the expenditure illustrated in Figure 2 covers only a proportion of the financial year. Administration and management includes staff salaries, Board costs and consultancy fees. Three grants were awarded in September 2004 and expenditure to March 2005 is shown in Figure 2. Communications includes branding, advertising and initiation of the development of the NC3Rs website. Programmes include, for example, the annual stakeholder meeting, animal technician symposium and various working groups.

The total expenditure for September 04 to March 05 was £303,364. Total expenditure between April 2004 and August 2004 was £61,033. This expenditure related to operating costs of the Centre for Best Practice for Animals in Research prior to its replacement by the NC3Rs. Unspent income of £331,603 was carried forward to the next financial year. The NC3Rs is grateful to the MRC for providing office space and infrastructure support including IT, payroll and personnel services.

An independent accountant has been appointed to oversee the management of the NC3Rs finances. For logistical reasons the NC3Rs uses the MRC accounting systems and the Centre is therefore subject to its auditing procedures.

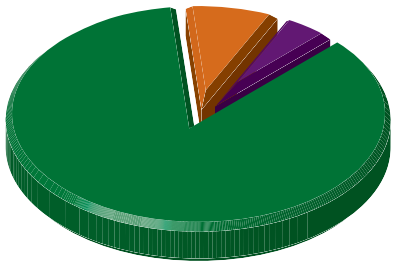


Fig 1

Income for April 04 - March 05	
MRC	£600,000
BBSRC	£61,000
Home Office	£35,000
Total Income	**£696,000**

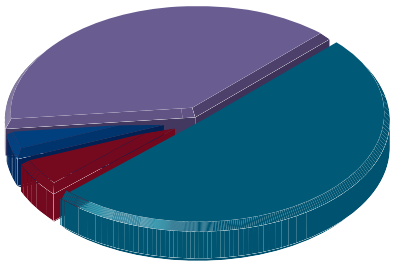


Fig 2

Expenditure for Sept 04 - March 05	
Administration & Management	£153,021
NC3Rs Research grants	£118,379
Communications	£18,435
Programmes	£13,529
Total expenditure	**£303,364**

Looking ahead

Since April 2005 the NC3Rs has secured additional funds from the Government, ABPI, GSK, the Wellcome Trust and LASA.

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