



# Fund for the Replacement of Animals in Medical Experiments

## Annual Report and Review 2005–2006

### Ten Achievements of FRAME for 2005–06

- 1 Development of the concept of invalidation to avoid unnecessary work being directed toward developing and validating inherently inadequate and unsuitable new test methods.
- 2 Organising an expert workshop on risk assessment.  
Publishing a special issue of *ATLA* on the REACH chemicals testing legislation, focusing on publications arising from the FRAME initiative on this issue.
- 3 Completion of the ECVAM/FRAME/CRUK collaborative validation study on using basal cytotoxicity in tissue cultures to predict the toxicity of anti-cancer agents.  
Successful lobbying of the European Commission to:
  - a) adopt intelligent testing strategies for chemicals testing; and
  - b) to facilitate the development and validation of alternatives for botulinum and shellfish toxin testing.
- 4 The production of an extensive resource for the use of serum-free tissue culture media to avoid painful procedures to obtain serum from calves.
- 5 Production of a submission to the Health & Safety Executive Round Table Discussion on the EU Physical Agents (EMF) Directive (EU Directive 2004/40/EC), highlighting concerns about its impact on laboratory animal experimentation.
- 6 Writing a comprehensive workshop report for ECVAM on the use of biotransformation systems with *in vitro* test methods
- 7 The formulation of recommendations for improving animal Project Licence Abstracts, on the Home Office website to increase public understanding of why animal experiments are necessary, and how they are regulated.
- 8 Participation in the *5th World Congress on Alternatives* (Berlin, August, 2005) with scientific presentations and an exhibition stand.
- 9
- 10





# Development Activities

FRAME's Research Programme is continuing to be conducted at both the FRAME office and in the FRAME Alternatives Laboratory (FAL) and the Molecular Toxicology Laboratory (Medical School, University of Nottingham). Work at the FAL is beginning to diversify with the appointment of a new director, Dr Andrew Bennett.

Progress with the development of improved organotypic skin and eye models for the safety testing of cosmetics and toiletries, as well as the development of models of embryotoxicity by using embryonic stem cells, has continued. New laboratory work has been initiated to develop a human cell tissue bank, in conjunction with clinicians within the Queen's Medical Centre. Initially, this is focusing on liver cells, obtained from patients with informed consent and according to ethical guidelines. Genetically engineered cell lines are being developed from these primary cells as well as tools for undertaking biomedical research and testing without using animals.

The research project at the University of the West of England, on the development of an *in vitro* model of the lung for investigating the toxicity of inhaled substances, continues to yield interesting and relevant data. The outcome of an international interlaboratory collaborative trial, in which the FAL participated to validate tissue culture methods for reducing and eventually replacing animals used for determining the acute toxicity of substances, is shortly to be published, and has been deemed a success.

The FAL's involvement in the multi-centred EU-funded Acute-Tox project, investigating the use of basal cytotoxicity data from cells in tissue culture to predict human acute toxicity, is continuing. A further collaboration with Cancer Research UK, involving similar methodologies to predict the toxicity of a range of anti-cancer drugs, has been successfully completed.

The Molecular Toxicology Laboratory has now completed a project to develop a high throughput



screening system based on the use of heat shock protein as an early marker of gene expression.

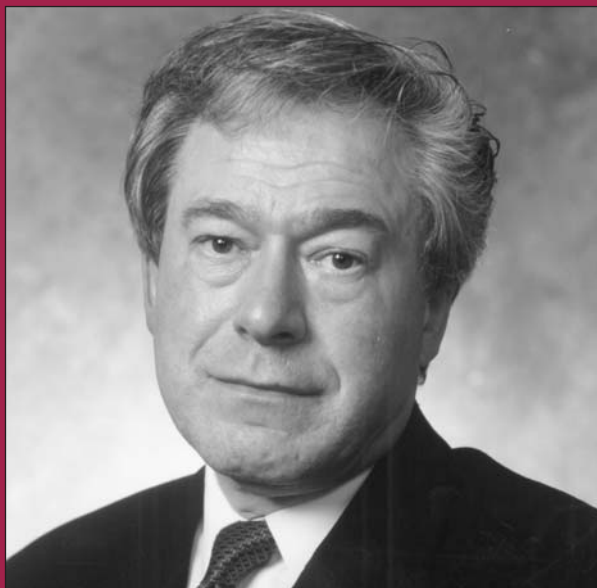
Research in the FRAME office has been focused on the new EU chemicals testing legislation (called REACH) with respect to its implications for increased animal testing and alternative methods. During the year, FRAME produced a special issue of its scientific journal, *Alternatives to Laboratory*

*Animals (ATLA)* on REACH. FRAME continues to exert pressure on international regulatory and legislative bodies to adopt intelligent testing strategies with the maximum use of non-animal approaches. FRAME also continues to campaign for improvements to the OECD test guidelines for human health assessment.



Progress is continuing to be made via FRAME's collaboration with the pharmaceutical industry to address the issue of using dogs in laboratories, the results of which are being presented at scientific meetings and published in the scientific literature. During the year, FRAME formally launched a new project aimed at developing a realistic strategy for completely phasing out the use of non-human primates without compromising essential research and testing. The charity is also carrying on with its work in several other areas including: a) botulinum toxin and shellfish toxin testing; b) genetically modified animals; and c) endocrine disruptors (EDs).

The work of the FRAME Reduction Steering Committee and the FRAME Toxicity Steering Committee continues, with new projects either started or being planned.



Sadly, Lord Stratford (Tony Banks), a Patron of FRAME and Chairman of the All Party Parliamentary FRAME Group, died suddenly on 8 January 2006, whilst on holiday in Florida

FRAME scientific staff have participated in, and helped to organise several workshops and meetings, including one on *Possibilities for a New Approach to Chemicals Risk Assessment*, and another to mark the retirement of the former director of the FAL, Dr Richard Clothier; on *Developing and Using Tissue Culture Models of Human Toxicity*. The First Bill Annett Lecture (formerly the Annual FRAME Lecture) was given, at the Kennel Club, London by Dr Julia Fentem (Unilever), on *Working Together to Respond to the Challenges of EU Policy to Replace Animal Testing*.

FRAME has continued to lobby the UK Government, and other legislative bodies, about animal experimentation and alternatives, particularly via the All Party Parliamentary FRAME Group, and via its newsletter, *FRAME News*. In addition, FRAME has embarked on a initiative to update all its educational material, and to produce new leaflets to reflect changes in legislation and the development of new technologies. The new FRAME website is scheduled to be ready by the end of 2006.

During the year, 28 research papers were published in the scientific literature and 31 presentations were given at scientific meetings and workshops, arising from the FRAME Research Programme.

## Frame Presentations

April 2005—March 2006

A number of talks have been given at a wide variety of meetings, including the joint conference of the British Endocrinology Societies, an Institute for International Research (IIR) conference on *Implementing REACH*, a conference organised by the Society for Chemistry in Industry on *in silico* prediction, and one on developmental

neurotoxicity, held in Washington. A total of 16 presentations were also given at the 5th World Congress on Alternatives and

Animal Use in the Life Sciences, held in Berlin in August, 2005. In addition, FRAME has contributed to several debates and workshops on animal experimentation, and also gave an update on alternatives at a Home Office Inspectors conference.



Michael Balls and Julia Fentem at the First Bill Annett Annual Lecture



# Publications

## 1 April 2005—31 March 2006

Balls, M. & Combes, R. (2005). The need for a formal *invalidation* process for animal and non-animal tests. *ATLA* **33**, 299–308.

Balls, M. & Combes, R. (2005). Validation at a crossroads. *ALTA* **33**, 187.

Balls, M. (2005). The dependence of the happiness of superstar scientists on the freedom to conduct animal experiments. *ATLA* **33**, 437–438.

Balls, M. (2005). *The Ethics of Research Involving Animals: The report of the Nuffield Council on Bioethics, May 2005*. *ATLA* **33**, 649.

Balls, M. (2005). Alternatives to animal experiments: serving in the middle ground. *AATEX* **11**, 4–14.

Balls, M. & Combes, R. (2006). Applying the three Rs to animal experimentation and animal testing: are we merely drifting or lying at anchor? *ATLA* **34**, 1–2.

Balls, M. & Combes, R.D. (2006). The OECD health effects test guidelines: a challenge to the sincerity of commitment to the three Rs. *ATLA* **34**, 105–108.

Balls, M. & Stephens, M. (2006). Time for alternative action. *Soap, Perfumery & Cosmetics* **79(2)**, 32–33.

Bhogal, N. (2005). The EU REACH system: blessing in disguise or a wolf in wolf's clothing? *ATLA* **33**, 81–82.

Bhogal, N., Grindon, C. & Combes, R. (2005). Revolutionising the testing of medicines and chemicals in Europe. *AV Magazine*, 18–19. A publication of the American Anti-Vivisection Society. Spring 2005.

Bhogal, N., Grindon, C., Combes, R. & Balls, M. (2005). Toxicity testing: creating a revolution based on new technologies. *TRENDS in Biotechnology* **23**, 299–307.

Bhogal, N., Hudson, M., Balls, M. & Combes, R.D. (2005). The use of non-human primates in biological and medical research: evidence submitted by FRAME to the Academy of Medical Sciences/Medical Research Council/Royal Society/Wellcome Trust Working Group. *ATLA* **33**, 519–527.

Coecke, S., Ahr, H., Blaauboer, B.J., Bremer, S., Casati, S., Castell, J., Combes, R., Corvi, R., Crespi, C.L., Cunningham, M.L., Elaut, G., Eletti, B., Freidig, A., Gennari, A., Ghersi-Egea, J-F, Guillouzo, A., Hartung, T., Hoet, P., Ingelman-Sundberg, M., Munn, S., Jassens, W., Ladstetter, B., Leahy, D., Long, A., Meneguz, A., Monshouwer M., Morath, S., Nagelkerke, F., Pelkonen, O., Ponti, J., Prieto, P., Richert, L., Sabbioni, E., Schaack, B., Steiling, W., Testai, E., Vericat, J-A. & Worth, A. (2006). Metabolism: a bottleneck in *in vitro* toxicological test development. The report and recommendations of ECVAM Workshop 54. *ATLA* **34**, 49–84.

Combes, R. & Balls, M. (2005). Intelligent testing strategies for chemicals testing – a case of more haste, less speed? *ATLA* **33**, 289–297.

Combes, R. (2005). “Europe goes alternative” — what’s all the fuss about? *ATLA* **33**, 549–552.

Combes, R.D. (2005). Assessing risk to humans from chemical exposure by using non-animal test data. *Toxicology in Vitro* **19**, 921–924.

Combes, R. & Balls, M. (2005). Opportunities for the government to actively promote the three Rs during the UK’s presidency of the European Union (1 July to 31 December 2005). *ATLA* **33**, 317–311.

Farzaneh, P., Allameh, A., Pratt, S., Moore, N., Travis, L., Gottschalg, E., Kind, C. & Fry, J. (2005). Increased heat shock protein 70 expression following toxicant-mediated cytotoxicity: A ubiquitous marker of toxicant exposure? *ATLA* **33**, 105–110.

Grindon, C. & Bhogal, N. (2005). The fourth EC report on the statistics of laboratory animal use: trends, recommendations and future prospects. *ATLA* **33**, 417–426.

Grindon, C., Bhogal, N., Combes, R. & Balls, M. (2005). The scientific, animal welfare and regulatory implications of the EU REACH system for chemical safety. *TOPRA Regulatory Rapporteur* **2**, No. 4, 16–22.

Grindon, C. & Combes, B. (2006). Introduction to the EU REACH legislation. *ATLA* **34**, Suppl. 1, 5–10.

Grindon, C., Combes, R., Cronin, M.T.D., Roberts, D.W. & Garrod, J. (2006). A review of the status of alternative approaches to animal testing and the development of integrated testing strategies for assessing the toxicity of chemicals under REACH — a summary of a DEFRA-funded project conducted by Liverpool John Moores University and FRAME. *ATLA* **34**, Suppl. 1, 149–158.

Hudson, M. & Bhogal, N. (2006). An analysis of the Home Office Statistics of scientific procedures on living animals, Great Britain 2004. *ATLA* **34**, 85–103.

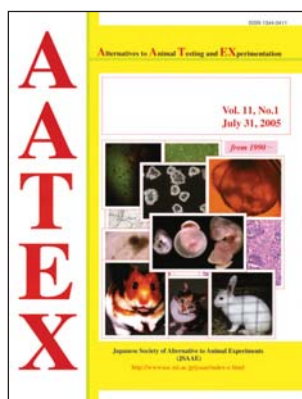
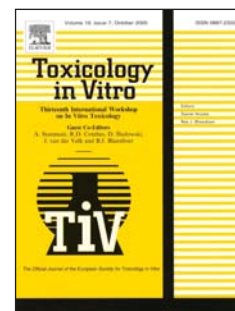
Hudson, M., Bhogal, N. & Balls, M. (2005). The use of non-human primates in regulatory toxicology: comments submitted by FRAME to the Home Office. *ATLA* **33**, 529–540.

Hudson, M. (2005). The welfare and scientific advantages of non-invasive imaging of animals used in biomedical research. *Animal Welfare* **14**, 303–317.

Moore, P., Ogilvie, J., Horridge, E., Mellor I.R. & Clothier R.H. (2005). The development of an innervated epithelial barrier model using a human corneal cell line and ND7/23 sensory neurons. *European Journal of Cell Biology* **84**, 581–592.

Morales, A.H., Perez, M.A.C., Combes, R.D. & Gonzalez, M.P. (2006). Quantitative structure activity relationship for the computational prediction of nitrocompounds carcinogenicity. *Toxicology* **220**, 51–62.

Wilkinson, P.J. & Clothier, R.H. (2005). Comparison of an animal product free medium and normal growth supplement on growth and barrier integrity of a human corneal epithelial cell line. *ATLA* **33**, 509–518.



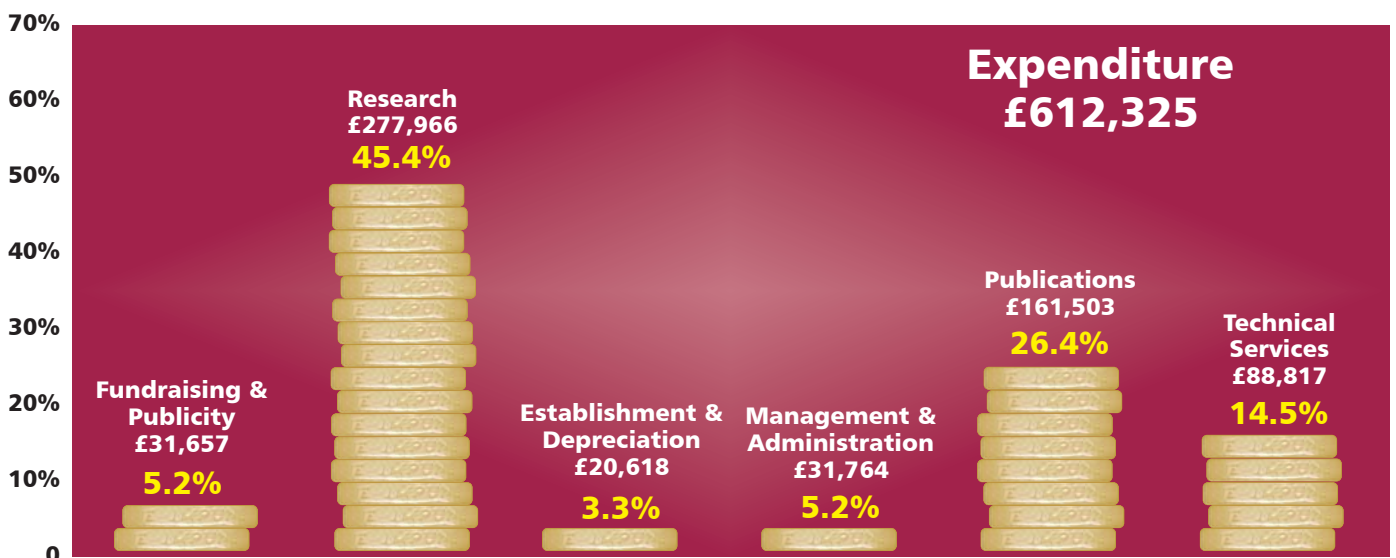
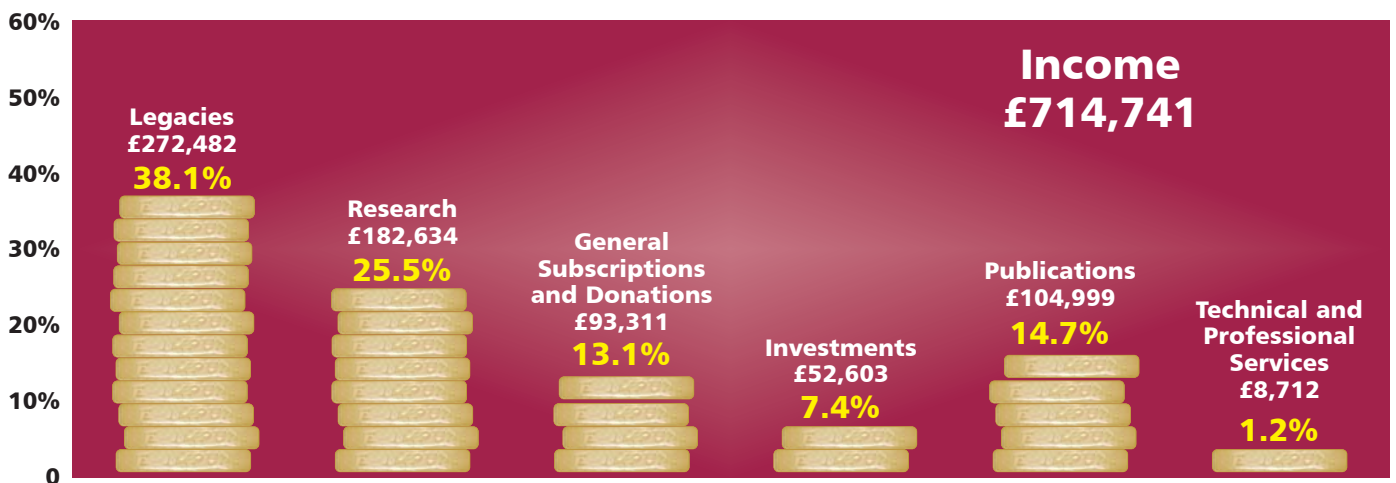


# Financial Review

## 1 April 2005—31 March 2006

**FRAME maintained the high level of financial support to further the aims of the charity by spending 86% of its overall expenditure on research projects, technical support services and scientific and educational publications. Almost £530,000 was spent in these three major activities out of a total expenditure of £612,000. Management and administration costs were kept at very low level of 5.2% (£32,000) of the total expenditure for the year.**

Funding for FRAME's research programme is reliant on donations which have sadly, fallen for the second year running, by a further 13%. It must be acknowledged that it is important to obtain sufficient and regular income from larger corporate supporters to fund core research activities at the FRAME Alternatives Laboratory in the University of Nottingham. Trustees are in constant communication with current and potential new donors to encourage the support of the alternatives programme.





# Financial Review

1 April 2005—31 March 2006



FAL laboratory

FRAME's corporate membership scheme aimed at smaller industrial supporters remains a useful source of income, although there has been a slight decrease in revenue over the previous year, but it is hopeful that, by continued encouragement, more companies will wish to support the aims of FRAME.

FRAME has managed to support its research programme to a level greater than the research donations allowed, due to the income from legacies. This year £272,500 was received from legacies, compared with £115,400 in the previous year. Trends in legacy income are notoriously difficult to predict and long-term research programmes cannot be planned on the basis of receiving legacy income at a certain level in a given year.

*ATLA* (Alternatives To Laboratory Animals) is the journal published by FRAME and provides an important conduit of ideas and publications of scientific research into alternatives to the use of animals in experimentation. The production of the journal involved a high level of activity throughout the year, with the publication of two supplements; *Alternative (Non-Animal) Methods for Cosmetics Testing: Current Status and*

*Future Prospects and The REACH System: Scientific and Animal Welfare Implications of EU Legislation on Chemicals Testing.* These were in addition to the standard six issues.

Costs of publishing the journal are maintained by subscriptions, special donations and financial support from FRAME funds.

Throughout the year, FRAME provided technical and scientific advice usually free of charge to government and non-government organisations. The technical department created educational and information leaflets on specific and current issues and published and presented papers in their areas of expertise at world congresses and conferences.

To maintain financial security for the charity, FRAME has, in the past invested some of its donations and legacies, and has a broad-based investment portfolio which is reviewed quarterly. By the year-end, there was a rise of £119,800 in the overall value of investments. This, in conjunction with the annual £102,400 surplus of income over expenditure, resulted in a balance sheet rise of £222,200, bringing the total to £1.546 million. FRAME aims to protect the capital of its endowed funds, but it draws on investment income generated from them, to bridge the gap between income and expenditure in any year when there is a deficit of income over expenditure in order to maintain its commitment to research into alternative testing.

FRAME's investment policy protects the financial assets of the charity, by means of a prudent and cautious approach to a choice of investment portfolio which is designed to meet the future needs of the charity in the short, medium and long-term, in terms of both capital and income.



# Donations and Legacies

1 April 2005—31 March 2006

## FRAME Corporate Membership

### Five-star members

These are companies which donated an annual sum of £20,000 or more. These companies may collaborate with FRAME in specific or general research projects, or contribute to the general funding of FRAME.

British American Tobacco  
Unilever



### Three-star members

These are companies which donated an annual sum of £10,000 to £20,000. These companies may collaborate with FRAME in specific or general research projects or contribute to the general funding of FRAME.

Asda Stores Ltd  
AstraZeneca UK Ltd  
Avon Products Inc.  
The Boots Company plc  
Kimberly Clark Ltd  
Procter & Gamble UK Ltd  
Reckitt Benckiser plc  
J Sainsbury plc  
Shell International Ltd  
Tesco Stores Ltd  
Unilever UK Home and Personal Care



### Two-star members

These are companies which donated an annual sum of £5,000 to £10,000 either for a defined purpose or for general funding.

Coty UK Ltd  
GlaxoSmithKline Ltd  
The Kennel Club



### One-star members

These are companies which donated an annual sum of £1,000 to £5,000 either for a defined purpose or for general funding. Such donations are of particular value in providing money for activities such as education and publicity, which do not involve research.

British Association for Chemicals Specialities  
Charles River Laboratories  
Church & Dwight UK Ltd  
Colgate-Palmolive UK Ltd  
A & E Connock (Perfumery & Cosmetics) Ltd  
Covance Laboratories Ltd  
PZ Cussons (UK) Ltd  
Ecover (UK) Ltd  
Firmenich UK Ltd  
GE Healthcare  
Givaudan UK Ltd  
Huntingdon Life Sciences Ltd  
Johnson & Johnson Ltd  
SC Johnson Ltd  
Marks & Spencer plc  
Merck Sharp & Dohme Ltd  
Mercona (GB) Ltd  
Next plc  
Novo Nordisk A/S  
Rohm & Haas France SAS  
SafePharm Laboratories Ltd  
Sanofi-Aventis  
Smith & Nephew Research Ltd  
Somerset Stores Ltd  
Swallowfield Consumer Products Ltd  
Thor Group plc  
Waitrose Ltd



## Donations from Trusts

FRAME gratefully acknowledges the support of the following Trusts, from which a total of £28,515 was received during the year:

John and Susan Bowers Fund  
Basil Brown Charitable Trust  
The Buccleuch Charitable Foundation  
The Buckingham Trust  
The Marjorie Coote Animal Charities Trust  
Mrs H L Grimwade Charitable Trust  
The Innominate Trust  
Dolly Knowles Charitable Trust  
The Rufford Maurice Laing Foundation  
The Millar Foundation  
Sylvanus Charitable Trust  
The Toye Charitable Trust  
Walker 597 Trust  
The Uxbridge Charitable Trust  
The Barbara Welby Trust  
Mr & Mrs O J Whitley Charitable Trust  
The Leslie Williams Trust  
The D M & J Wood Deposit Trust

## Legacies Bequeathed to FRAME

Legacy Income during the year totalled £272,482. FRAME received bequests from the following supporters:

Mr Robert H Bradshaw, of Sleaford  
Miss Mollie A Burton, of Eastbourne  
Mrs Mina I A Dyer-Fane, of Worthing  
Miss Penelope J B Hetherington, of Southwold  
Mrs Joan Lewis, of Birkenhead  
Mrs Isobel W MacGregor, of Richmond  
Miss Audrey F O'Leary, of Portsmouth  
Major Hugh H Orpen, of Horsham  
Mrs Kathleen F Phelan, of Herne Bay  
Miss Mabel J S Pinwill, of Lewes  
Ms Audrey D Rushworth, of Mexborough  
Miss Helen M Scrimgeour, of Newport on Tay

## Donations in Memoriam were received from

Miss Jean Kerr, in memory of Mrs Maud Hemming.  
Mr Michael T Deans, in memory of Madge Worthington.  
J H Whitley, in memory of Mrs Marta Annett

## Donations in Memory of Mr Stuart John Elliott, were received from:

Mrs M Elliott, his wife  
Mr & Mrs P G Duggleby  
Mr & Mrs E C Dalley & family  
Mrs M Watson

# FRAME Office Scientific Staff



Zoology. Her main research interests are the application and promotion of methods to reduce the number of animals used in experiments, the refinement of animal procedures through non-invasive imaging and the training of animals. Michelle is also undertaking research to develop a strategic plan to allow the replacement of all non-human primates in biomedical research and testing.

**Nirmala Bhogal** (Science Manager) has a first degree in Biochemistry and Pharmacology and a PhD in biochemistry and Molecular

biology from Leeds University, where she specialised in rational drug design and protein chemistry. Before joining FRAME,



Nirmala undertook a Postgraduate Diploma in Law. Her current areas of research are the use of human volunteers and the application of biotechnology in alternatives research.

**Robert Combes** (Director) obtained a degree in Botany and a PhD from Queen Mary College, London. After undertaking research in genetic, biochemical and cellular toxicology in academia and industry, he joined FRAME in 1994 where he has focused on all aspects of applying Replacement, Reduction and Refinement strategies to biomedical research and testing.



After gaining a degree in Biomedical Science at the University of Bradford, **Elizabeth Donovan** (Publications Officer) worked at the Forensic

Science service for a year, then undertook a PhD in Molecular Biology at the University of Nottingham. Elizabeth then worked at Crookes Healthcare Ltd as a Medical Information Officer, before becoming Publications Officer at FRAME. Elizabeth's research interests include vaccine design and drug safety testing.

**Michelle Scrivens** (Scientific Officer) graduated from Nottingham Trent University with a degree in Physiology and Pharmacology, after which she obtained a PhD in Molecular Pharmacology there. Her current research interests are in



molecular toxicology, particularly the application of refinement and replacement to the use of transgenic animal models in toxicity testing.

**Christina Grindon** (Scientific Officer) has a degree in



Chemistry, Drug Design and Toxicology from the University of Hull and a PhD in Computational Chemistry from the University of Nottingham.

Her current research interests include molecular modelling, computational prediction systems and developing intelligent testing strategies for the new EU chemicals legislation, REACH.

**Michelle Hudson** (Scientific Officer) graduated from the University of Sheffield with a masters degree in

