

3R Research Foundation

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The 3R Research Foundation approved 20 projects and provided 2.8 million francs in grants in the 2000 to 2003 research period. The Foundation further promoted the principles of the 3Rs by disseminating information, providing training courses and creating an educational programme and making it available on Internet.

The projects financed in the period covered by this report dealt with all three aspects of the 3Rs, Reduce, Refine, Replace. The variety of research that can be done to further promote these principles is apparent from the list of projects. These stem from the basic biomedical research, pharmacology, toxicology and veterinary medicine sectors. Notable success has been achieved in substituting research models that use animals in clinical research with animal-free methods. In experiments to identify pollutants and in the development of potential new drugs, animals are saved by studying the relevant cell system mechanisms (interactions) rather than studying the effects on or injury to intact organisms.

Sixty-two grant applications were received from 2000 to 2003. Of these, 20 projects were approved and a total of 2.8 million francs provided in funds. Annually



From 2000 to 2003, the 3R Research Foundation provided almost 3 million Swiss francs in funding for research projects.

Reduce, Refine, Replace

The 3R Research Foundation was set up in 1987 by the Parliamentary Group for Animal Experiments, Interpharma¹ and the Fund for Animal-free Experimental Research. The Foundation is supported financially by the Swiss government – through its representative the Swiss Federal Veterinary Office – and by Interpharma. Equal contributions made by all parties are used by the Foundation to finance research to improve animal experiments (reducing pain or distress to animals), to refine experiments (less experiments, less animals used per experiment) or to avoid experiments through use of alternatives. These efforts are summed up in the 3R concept (Reduce, Refine, Replace).

The members of the Foundation's Board are drawn from the Federal Parliament, Interpharma, the Federal Veterinary Office and animal welfare organisations. The Board determines the priorities for research and selects suitable projects for support with the assistance of an eight-member evaluation committee and the Foundation's scientific advisor.

Since its inception in 1987, the Foundation has considered grant applications for 265 projects of which 90 projects were approved and financed to the extent of 12.3 million francs. Thirty percent of the projects submitted were approved and supported. The reason for the high number of rejections is to found not only in the scientific quality of the submitted projects but in whether the aims of the projects were in harmony with the Foundation's aims, that is to promote the principles of the 3Rs. Ninety-five percent of research grants were awarded to universities, of which more than 90% of funding was provided to Swiss universities and the rest to other European universities.

¹ Association of Pharmaceutical Research Companies in Switzerland: Novartis, Roche and Sero

between four and six projects are approved which run for one to three years. Each year contributions were made to between 10 and 12 ongoing projects. The number of grant applications is increasing. Rapid developments in the field of molecular biology and new analytical methods may be the explanation for this increase as these offer new approaches to realising the 3R principles.

A summary list of all new projects and the findings achieved to date (publications) are presented in English on the Foundation's website at www.forschung3r.ch. Some of these are shown in the following table classified according to experimental sector.

An expert is appointed to supervise each project and to co-operate with the scientific advisor to ensure research goals are achieved, he/she reads the interim research reports and if necessary liaises with the project leader. Once the results are published in a scientific journal the Foundation views projects as concluded.

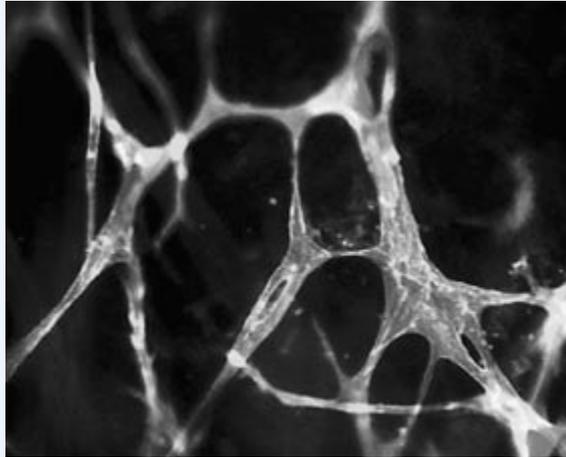
The Foundation uses this procedure to promote the use of findings in practical research. Ideally, this would lead to recognition of 3R methods by registration authorities or worldwide application of animal-free experimentation methods in biomedical and pharmaceutical research and development because published 3R research findings have to be taken into account when applications for animal experiments are being considered.

Public relations and training

Once again, in the period covered by the report, efforts focussed in particular on informing those individuals actually involved in animal experimentation, i.e. those who are in a position to improve the situation and have the 3R principles implemented, about what is being done to implement findings and about successful research projects. Information for specific target groups was offered on the Internet and in bulletins, the Foundation assisted in arranging training courses and an educational programme entitled the 3R Training Course was made available on the Internet. Through its participation in ecopa, the Foundation is associated with a European network of institutions with mutual aims.

Internet website: The 3R Foundation maintains its own Internet website - www.forschung3r.ch. In two or sometimes three languages the site informs interested parties about its aims and all current research projects; grant application papers can be downloaded and project report forms filled in online by project leaders. Presenting the projects on the Internet, where they are universally accessible, ensures international recognition for Switzerland's efforts in the 3R field. As already mentioned, the website is a tool for corresponding with grant applicants and project leaders.

Around 90 projects are presented with a summary of the project background, the methodology being used, findings to date and the influence of such on the implementation of the principle of the 3Rs. Many of the summaries are illustrated; references to where results have been published are updated periodically. In conjunction with the site search function this collection of data becomes a useful source of information on 3R methods. Three aims are being pursued by making this information available worldwide: 1) to encourage ideas among potential project leaders and to lay down the scientific standard for projects; 2) to provide information about Swiss 3R research to organisations with mutual goals and to the ECVAM (European Centre for the Validation of Alternative Methods); 3) to inform animal protection organisations about ongoing efforts to implement the 3Rs.



Formation of new blood vessels in the heart, an important factor in cardiovascular disease, was studied in cell cultures. Information could thus be gained that otherwise would have had to be obtained in painful animal experiments.

3R-Info-Bulletin: Twelve 3R Info Bulletins (ISSN 1421-6590) were published in the period of the report. Findings from successful projects funded by the Foundation are published in this A3-size brochure and sent to 900 recipients. The target public consists of potential grant applicants, specialists in animal experiments, animal protectionists and course participants. The brochure is published in English to increase its acceptability in research and development laboratories. The bulletins can be consulted on the Foundation's website. The feedback to the Foundation about the bulletin is positive.

Training courses: In Switzerland, all individuals who carry out authorised animal experiments are required to participate in a one-week training course to learn how to handle experimental animals in a responsible and caring manner and gain the needed skills. In recent years the Foundation's scientific advisor has explained the 3R principles to participants at training courses (LTK module 1) and other ongoing training for specialists and demonstrated to working groups how such could be implemented. During such courses, researchers were informed about the Foundation's grant arrangement for 3R projects and encouraged to submit their projects for consideration.

The "3R Training Course" Internet programme: The Foundation has created the 3R Training Course, a course available on Internet, for the benefit of all individuals charged with performing or supervising animal experiments. The Foundation is indebted to the authors without whose assistance (for which no fees were charged) the project could not have been realised. A training programme in two languages was created to inform users about alternatives to animal experiments in a project led by Prof. Dr. P Maier, the Foundation's scientific advisor, with the co-operation of Oekosophie GmbH, Basle, who took care of software

development; the training course can be obtained at www.tierversuch.ch using any PC with Internet access. The Association of Cantonal Veterinarians has adopted the programme into its animal protection legislation training course.

A major feature of the programme is the test that can be taken and submitted online; this is then evaluated and the participant receives confirmation of having taken the course. The Internet has great potential in this respect as the course can be arranged in a flexible manner and be corrected or extended in line with the practical experience and needs of users. This is the first time such a teaching programme has been made available in this field.

ecopa – Association for the promotion of the principles of the 3Rs

In the autumn of 2002, in Brussels, ecopa (European Consensus Platform for 3R Alternatives to Animal Experimentation) was formally founded as an association with the assistance of the Foundation, and the Foundation was granted membership. Ecopa is an association of European organisations representing the four interest groups industry, government, universities and animal protectionists that have united to mutually promote the principles of the 3Rs. One organisation per country is adopted as a member. Eleven countries are participating currently: these are Austria, Belgium, Britain, the Czech Republic, Denmark, Finland, Germany, The Netherlands, Italy, Sweden, Switzerland.

At the Fourth Annual General Meeting in 2003 the Foundation's scientific advisor was elected to the committee of ecopa. Thus the Foundation represents Switzerland and is actively integrated in European efforts to promote the 3R principles (ECVAM) and is the initial contact for foreign institutions that wish to use 3R research methods.

Further information can be obtained from the secretariat of the 3R Research Foundation, CH-3110 Münsingen (e-mail: secretary.3R@bluewin.ch). For information about grant applications or projects, contact the Foundation's scientific advisor (e-mail: research.3R@bluewin.ch). ■

3R projects in the period from 2000 to 2003

Research to replace animal experiment models that cause distress:

Infection model

- A non-mammalian system to study bacterial infections (Cosson P., Centre Médical Universitaire, Geneva)

Septic shock

- Generation and functional characterization of a clonal murine periportal Kupffer cell line from H-2Kb-tsA58 mice (Landmann R., Infectious Disease Department, Department of Research, University Hospital, Basle)

Replacement methods for toxicological testing or for testing the pharmaceutical effects of potential medicines:

- Induction of a primary T-cell mediated immune response against drugs and drug metabolites *in vitro* (Pichler W.J., Allergy Department, University Hospital, Berne)
- Internet laboratory for predicting harmful effects triggered by drugs and chemicals (Vedani A., Biographics Laboratory 3R, Basle)
- *In vitro* replica of the inner surface of the lungs, for the study of particle-cell interaction (Geiser Kamber M., Anatomical Institute, University of Berne)
- Validation of combined perfusion/loading chamber for *ex vivo* bone metabolic studies and biomaterial interactions (Richards R.G., A.O. Research Institute, Davos)

Alternative methods in biomedical research:

- Development of a model of heart angiogenesis *in vitro* (Battagay E., Outpatient Department of Internal Medicine and Department of Research, University Hospital of Basle)
- The development of an *in vitro* intervertebral disc organ culture system (Lee C., Biochemistry and Cell Biology Unit; A.O. Research Institute, Davos)
- *In vitro* model for the testing of endothelial cell activation and damage in whole blood (Rieben R., Heart Transplantation Laboratory, Cardiology, University Hospital of Berne)
- Direct cloning of human antibody cells from purified B-cells (Wirthmüller U., Institute of Immunology, University Hospital, Berne)

Reduction of distress in animals used for research and development of medicines:

- Magnet Resonance Imaging (MRI) for the non-invasive assessment of lung inflammation and pulmonary function in the rat (Beckmann N., Novartis Institute for Biomedical Research (NIBR), Novartis Pharma AG Basel)

Replacement of host animals in research into infectious veterinary medical disease:

- Development and applications of an *in vitro* cultivation model for *Neospora caninum* tissue cyst formation (Hemphill A., Institute for Parasitology, University of Berne)
- Development of an *in vitro* culture model to generate *Neospora caninum* and *Toxoplasma gondii* oocysts and sporozoites (Hemphill A., Institute for Parasitology, University of Berne)
- *In vitro* screening methods for repellents and attachment deterrents for ticks (Guerin P., Institute of Zoology, University of Neuchâtel)
- Validation of polymerase chain reaction assays as replacement of the mouse and rat antibody production (MAP/RAP) (Bootz F., Institute of Laboratory Animal Science, University of Zurich)

Improving experimental methods and husbandry of animals:

- Assessing animal health and welfare and recognising pain and distress (Flecknell P., Comparative Biology, Centre University of Newcastle)
- Reproducibility and external validity of findings from animal experiments: influence of housing conditions (Würbel H., Institute of Laboratory Animal Science, University of Zurich)
- Detection and characterisation of signs of pain in mice by the combined use of a telemetry model and behavioural observations (Arras M., Institute of Laboratory Animal Science, University of Zurich)

Improving cell culture methods:

- Information on serum-free cell lines, an interactive database (Strebel C., CePower GmbH, Wädenswil)