

**3R Research Foundation Switzerland**

*Annual Report* | **2012**

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**3R-Principles**

The 3Rs are Replace, Reduce and Refine animal experimentation. The 3Rs must be the guiding principles behind animal experimentation; if a study can be carried out without using any laboratory animals then such a procedure must be used. If it is essential to use laboratory animals under the terms of animal protection legislation the number used must be kept to a strict minimum. The third "R" requires that animals used for laboratory experiments be made to suffer an absolute minimum of pain and/or stress. The 3R Research Foundation funds research projects whose aim is to improve present-day experimental methods from the point of view of the 3Rs.

**The 3R Research Foundation in 2012**

In 2012 the Foundation provided a total of CHF 618,767.15 for 14 research projects. The Confederation and Interpharma made a total contribution of CHF 1,020,000.–. The Administrative Board approved 4 new projects, while 4 projects were successfully completed. In view of the limited funds available, the call for projects was restricted to one deadline only, namely in February 2012. Furthermore, a new 2-stage application procedure was introduced. Out of the 13 project proposals submitted the Evaluation Committee selected 6 that were more relevant to the 3R principles and asked those applicants to submit a detailed description of their projects. A further selection process eliminated two projects whose relevance to the 3R principles was less evident, there being insufficient funds in the Foundation's coffers for all six. The 3R Info Bulletins 48–50 included the results of two completed projects. On the 25<sup>th</sup> anniversary of the creation of the Foundation, some thoughts about the activities and the future role of the Foundation were also presented.

To mark its 25<sup>th</sup> anniversary in 2012, the Foundation organised a scientific workshop together with the Swiss Laboratory Animal Science Association, and with the collaboration of the Swiss Toxicology Association, in November in the Technopark in Zurich. During this workshop, ecopa (European Consensus Platform for 3R Alternatives to Animal Experimentation) held its annual general meeting. The workshop was attended by 400 specialists in the field of animal experimentation and alternative methods.

The future direction of the Foundation's activities was the focus of further debate among the Administrative Board. In May the Foundation had the opportunity to give a presentation to the National Council's Committee for Science, Education and Culture in which it described developments in animal experimentation. The Scientific Advisor, Prof. Peter Maier, retired at the end of the year. The Administrative Board offered him their very best wishes for the future, and were lucky enough to be able to replace him by Prof. Ernst B. Hunziker from the University of Berne.

**The Administrative Board**

The Administrative Board of the Foundation is made up of nine members, two representing the Swiss parliament (1 seat vacant), two representing animal protection, two from Interpharma and two from the Federal Veterinary Office, as well as a representative of other interested circles. Current members are:

Christine Egerszegi-Obrist  
member of the Council of States, Mellingen  
Chairwoman

Dr. Peter Bossard  
Horw, Deputy Chairman

Dr. Franz P. Gruber  
Doerenkamp-Zbinden Foundation,  
Küsnacht (until 31. 12. 2012)

Dr. Ingrid Kohler  
Federal Veterinary Office, Berne-Liebefeld

Dr. Markus Schmutz  
Novartis Pharma AG, Basle (as from 30.3.2011)

Silvia Matile-Steiner  
lawyer, Reinach

Dr. Markus Schmutz  
Novartis Pharma AG, Basle

Nathalie Stieger, economist  
F. Hoffmann-La Roche Ltd., Basle

Prof. Hans Wyss  
Director of the Federal Veterinary Office,  
Berne-Liebefeld

**The Evaluation Committee**

Prof. Peter Maier  
University of Zurich  
Chairman (until 31. 12. 2012)

Prof. Ernst B. Hunziker,  
University of Berne Berne (as from 1. 3. 2013)

Dr. Franziska Boess  
F. Hoffmann-La Roche Ltd, Basle

Prof. Clemens A. Dahinden  
Institute of Immunology and Allergology,  
University Hospital, Berne

Prof. Marianne Geiser Kamber  
Institute of Anatomy, University of Berne

Prof. Andrew Hemphill  
Institute of Parasitology, University of Berne

Prof. Simon P. Hoerstrup  
Swiss Center for Regenerative Medicine  
(SCRM), University and University Hospital  
Zurich (as from 17.1.2012)

Dr. Ingrid Kohler  
Federal Veterinary Office, Berne-Liebefeld

Dr. Kurt Lingenhöhl  
Novartis Pharma Ltd, Basle

Prof. Thomas Lutz  
Institute of Veterinary Physiology,  
University of Zurich

Dr. Martin Reist  
Sanisys Ltd, Biel (until 30. 4. 2013)

Dr. Stefanie Schindler  
Animalfree Research Foundation, Berne

**Scientific Adviser**

Prof. Peter Maier, University of Zurich  
(until 31. 12. 2012)

Prof. Ernst B. Hunziker, University of Berne  
(as from 1. 3. 2013)

**Administrator**

Ernst P. Diener, lawyer, Münsingen

**Auditors**

Waber Treuhand GmbH, Einigen

**Supervisory body**

Federal Department of Home Affairs

**Articles and statutes of the Foundation**

- Deed of foundation dated 13 February 1987, modified on 28 September 2011
- Regulations dated 30 March 2011
- Guidelines for awarding research grants dated 15 May 1987 (latest modification 7 May 2013)

## Summary of the Year's Activities

### The Foundation's website

Detailed information about all the Foundation's activities can be found on its website at [www.forschung3r.ch](http://www.forschung3r.ch).

Two more propositions for 3R-relevant methods were added to the section entitled "3R-Methods".

*Experimental colitis through serial assessment of disease activity by 18F-FDG PET/CT* Dr. Dominik Bettenworth, University Clinic Münster, Germany. Preclinical evaluation of potential drug candidates for human inflammatory bowel disease is performed in murine models of colitis. The most widely used model is dextran-sodium sulfate (DSS)-induced colitis. Non-invasive imaging of murine experimental colitis by Positron emission tomography (PET) combined with radiotracers is a feasible alternative and offers the opportunity of serial follow-up investigations. This technique significantly reduces the number of test animals required.

*Quantitative, non-destructive biofilm analysis on irregular surfaces using microcalorimetry* Dr. Martin Clauss, Orthopaedics Department, Cantonal Hospital, Liestal und Dr. Andrej Trampuz, University Hospital, Lausanne, Switzerland. This in-vitro approach allows the quantification of biofilm formation on implants, human bone grafts and bone-graft substitutes by means of microcalorimetry. The method has the advantage of allowing the detection of bacterial biomass without removing the biofilm from the surface of the specimen.

### 14 projects subsidised

A total amount of CHF 618,767.15 was paid out for 14 ongoing projects during 2012.

### Four new projects

Four new projects were approved in 2012 for which a total of CHF 472,039.– has been earmarked. These new projects are described in detail in the list of funded projects on the Foundation's website ([www.forschung3r.ch/en/projects/index.html](http://www.forschung3r.ch/en/projects/index.html)).

*Antibody phage selection strategy for application in non-specialized laboratories* (131/12) Prof. Christian Heinis, Laboratory of Therapeutic Peptides and Proteins, EPFL, Swiss Federal Institute of Technology Lausanne, Switzerland. Monoclonal antibodies for use in research continue to be produced using hundreds of thousands of rodents. The main reason for this is the complexity of the in vitro method and the limited use of commercially available phage libraries. In this project a new combination of techniques will be examined (high-throughput sequencing and DNA synthesis) with which the procedure can be carried out at a much lower cost. A sufficiently complex phage library should be made available to research laboratories without any restrictions and phage selection should be possible using fewer experimental steps. The simplified procedure could also be carried out in non-specialized laboratories. As a result, the simplification of antibody phage selection could help achieve a breakthrough in the application of this in vitro method, the principle of which has already been known to researchers for a number of years.

*Identification of predictive in vitro markers for hematopoietic stem cell function* (132/12) Prof. Matthias P. Lutolf, Institute of Bioengineering, EPFL, Swiss Federal Institute of Technology Lausanne, Switzerland. In order to test whether hematopoietic stem cells (HSC) are capable of producing normal blood cells over a longer period of time, they are normally implanted into mice. Measurements are then made to see whether the HSC are able to reconstitute the blood system that has been destroyed through radiation. This procedure causes extreme suffering to the animals used and a large number of mice have to be sacrificed. In this project, Prof. Lutolf and his team

intend to identify new cell markers to predict the long-term functioning of HSC that have been developed in vitro.

*Development of an in vitro system to grow and investigate vascular endothelial cells under physiological flow* (133/12) Prof. Robert Rieben, Department of Clinical Research, University of Berne, Switzerland. The function of endothelial cells in the walls of blood vessels is often investigated in vivo, causing suffering to the laboratory animals involved. Conventional in vitro procedures simulate the physiological conditions with inadequate accuracy. This new in vitro experimental method is aimed at replacing many such in vivo studies. In the proposed in vitro model the pressure and shearing power of the pulsating blood, for example, are simulated. This system should make it possible to find answers to questions concerning ischaemia, reperfusion and transplantation that have so far been investigated in in vivo experiments involving considerable pain and suffering for the laboratory animals concerned.

*Development of a cardiovascular simulator with autoregulation* (134/12) Prof. Stijn Vandenberghe, ARTORG Center for Biomedical Research, University of Berne, Switzerland. Many studies are carried out in vivo for testing and gaining regulatory approval for cardiological devices. The aim of this project is to adapt a cardiovascular simulator to in vivo conditions in such a way that far fewer laboratory animals are required for testing such devices as blood-pumps, for example. The challenge in this case is to simulate self-regulating, clinically relevant mechanisms such as baroreflex (blood pressure and heart beat regulation) and the Frank-Starling mechanism (correlation between inflow and expulsion). The (preliminary) testing of devices using such further developed simulators should help to ensure that only the most promising devices are tested in vivo.

#### Four projects successfully completed

*Engineering of a human brain tumor model to replace animal experimentation* (115/09) Prof. Olivier Preynat-Seauve, Department of Pathology and Immunology, University Medical Centre, University of Geneva, Switzerland. The aim of this project was to combine the delicate cell culture models developed by the project leader for brain tissue (engineered neural tissue, ENT, from embryonic stem cells) and glioblastomas (engineered glial tumors, EGT, from human tumor tissue), and thus to develop an in vitro system for studying glioblastomas and characterising their molecular structure. Such a system would replace in vivo methods that cause considerable suffering to the laboratory animals used, in particular in relation to the intracerebral or subcutaneous injection of human tumor cells in immuno-suppressed mice. The team were successful in establishing their in vitro system. Histo-pathological and molecular-biological studies were carried out on the reaction of the EGT transplanted into the ENT. It now remains to examine the various ways in which this model can be used.

*Development of non-invasive strategies to study spinal cord disease, injury and repair* (120/10) Prof. Denis Jabaudon, Neuroscience Department, University Medical Centre, University of Geneva, Switzerland. In this project, Prof. Jabaudon aimed to develop a method for the non-invasive injection of substances (e.g. plasmids) into the spinal cord of mice without using a surgical procedure. Such a method would result in a lower rate of mortality and less suffering among the laboratory animals used. The research team was able to demonstrate that the high-resolution ultrasound method for positioning the hypodermic needle for cortical injections was equally as accurate as the stereotactic method. On the other hand, the ultrasound method proved to be unsuitable for spinal injections. It was therefore not possible to establish the non-invasive injection method for use in the spinal cord.

*A new in vitro model to study therapeutic approaches to improve spinal cord regeneration and repair after injury* (121/10) Prof. Roman Chrast, Department of Medical Genetics, University of Lausanne, Switzerland. This project aimed to examine the effect of various substances on spinal cord regeneration in vitro using mouse organotypic longitudinal, sagittal slice cultures developed by the project leaders. The research team was also able to induce lesions similar to those seen in multiple sclerosis, thus allowing for functional and structural studies. Using this method it would be possible to avoid a large number of tests on live animals. Comparative in vivo and in vitro studies using potential new medicines remain to be carried out.

*Use of "moribund" stage in the acute fish toxicity test according to OECD guideline 203 and its effect on LC50 values* (123/10) Dr. Hans Ruffli, ecotoxolutions, Basle, Switzerland. The aim of this project is to define the final "moribund" stage in the acute toxicity test in fish in order to introduce it as a criterion for interrupting the test under OECD guideline 203. Retrospective analysis of data and protocols from hundreds of toxicity tests carried out on fish has shown that by introducing the "moribund" criterion the suffering of the fish through the acute effects of a test substance could be reduced by up to 92 hours thanks to its earlier removal from the test. By introducing the "moribund" criterion, the LC50 value could be lowered, on average by a factor of 2, in up to half of the experiments. Attempts are now being made, in collaboration with the Swiss Federal Office for the Environment and various EU countries, to get the OECD protocol changed. This would help to achieve a significant reduction in the level of suffering among the fish used in this test.

### 3R-Info-Bulletins

3R Info Bulletins are published on the Foundation's website ([www.forschung3r.ch/en/publications/index.html](http://www.forschung3r.ch/en/publications/index.html)).

*A novel ex vivo mouse aorta perfusion model* (Bulletin no. 48, February 2012) In this project, Prof. Patrick Hunziker, Clinic for Intensive Medicine, University of Basle, Switzerland and his research group have extracted and cultured ex vivo aorta tissue of transgenic (ApoE<sup>-/-</sup>) mice. A method was developed for obtaining the tissue and its subsequent on-line observation under a fluorescence microscope. It was possible to identify and characterise the sclerotic sections of the walls of the aorta (plaques) following perfusion of the aorta with specific markers. The time taken for changes to the cells could also be determined. The results obtained corresponded to a great extent to findings from studies using ApoE<sup>-/-</sup> mice, which shows that many studies, for example for preselecting potential new medicines, could be carried out ex vivo.

*Bacterial Meningitis: Investigating Injury and Regenerative Therapy in vitro* (Bulletin no. 49, June 2012) Bacterial meningitis (BM) causes brain injury in the dentate gyrus (DG) of the hippocampus, with bacterial components and the host organ's inflammatory reaction contributing jointly to the insult. The researchers, Prof. Stephen Leib and team from the Neuroinfection Laboratory at the Department of Clinical Research, University of Berne, Switzerland, succeeded in differentiating neural stem cells and precursor cells at different stages of development and simulating in them the reaction to the damaging effect of bacterial meningitis. It is likely that compromised brain areas can be repaired by grafting suitable stem/progenitor cells into brain tissue. This process has been successfully carried out in cultured brain slices in vitro. Thanks to the in vitro methods developed by the researcher, it will be possible in the future to carry out indicative preliminary examinations that are necessary to identify appropriate cells for transplantation, for example. It would only be necessary to use laboratory animals for the final confirmation of the in vitro findings.

*Still relevant twenty-five years on; 25 years of Funding the 3Rs* (Bulletin no. 50, December 2012)  
Prof. Peter Maier, Scientific Advisor of the 3R Research Foundation Switzerland until the end of 2012, reflects on the visibility, activities and future role of the Foundation. Dr. Stefanie Schindler, an animal welfare expert, assesses the Foundation's twenty-five years of funding. To mark the Foundation's 25<sup>th</sup> anniversary, the two authors describe the present situation with regard to animal experimentation in Switzerland (awareness of the Foundation's work, limited funds) and the progress achieved so far concerning reduction and refinement. In order to prevent an increase in the use of laboratory animals in the field of life sciences, the established research promotion involving live animals should specifically support aspects relevant to the 3R principles. A study is under way to analyse what the 3R Research Foundation has achieved over the past 25 years in various fields through its albeit limited funding; initial results are published.

## Legal form of the Foundation

The Foundation is a cooperative institution set up by the Parliamentary Group for Animal Experimentation Questions (public organ), Interpharma (association of pharmaceutical companies that carry out research, comprising at present AbbVie Ltd, Actelion Ltd., Amgen Switzerland Ltd, Bayer (Switzerland) Ltd, Boehringer Ingelheim (Switzerland) Ltd, Gilead Sciences Switzerland Ltd, Janssen-Cilag Ltd, Merck Serono International Ltd, Novartis Pharma Ltd, Pfizer Ltd, F. Hoffmann-La Roche Ltd, Sanofi-Aventis (Switzerland) Ltd, UCB Pharma Ltd and Vifor Ltd), and the Animalfree Research Foundation (animal protection). The Foundation was entered in the commercial register on 18 August, 1987.

The funds for subsidising research are provided principally by the Federal Veterinary Office and Interpharma.

## Purpose of the Foundation

The purpose of the 3R Research Foundation Switzerland is to promote alternative research methods through grants for research projects as well as to implement and promote the 3R principles. The organisation supports first and foremost projects aimed at developing new methods or refining accepted methods (validation) which offer improvements vis-à-vis standard animal experimentation in line with the 3R motto, Replace, Reduce, Refine.

A broad range of projects is funded on the condition that they are likely to replace animal experimentation or to reduce the number of animals used or the stress and/or pain suffered. Accordingly, projects based on the Foundation's three principles and covering any of a broad selection of bio-medical disciplines will be taken into consideration.

## Activities during 2012

In the Foundation's twenty-sixth year of existence the Administrative Board met five times, namely in January, March, August, October and December, for a half-day meeting. Apart from the statutory business concerning the end of the business year 2011, the Board addressed the following issues.

In January, the Board discussed personnel issues and the future direction of the Foundation's activities. At its March meeting it focused on the financial statements for 2011 and the earmarking of research funds for ongoing projects. In addition, discussions covered ways of instigating collaboration with the Swiss National Science Foundation (SNF) in order to persuade the latter to provide funds for research relevant to the 3R principles. The Administrative Board would like to see increased efforts in networking in order to achieve greater application of the 3R principles in scientific research.

At its meeting in August, the focus was on funding for new projects. Out of a total of 13 proposed projects, 4 were finally approved. The final reports on 4 completed projects were received. A decision was then taken regarding the procedure for advertising for a replacement for the Scientific Advisor, who would retire at the end of 2012. Finally, the Administrative Board was informed about how preparations for the 25<sup>th</sup> anniversary workshop were progressing; the event was to be organised together with the Swiss Laboratory Animal Science Association and would take place in Zurich on 19 and 20 November 2012. Information on the Foundation's 25<sup>th</sup> anniversary would be provided to the media and would be used to inform the general public about our commitment to animal protection and science. A number of successful projects would be presented in easily comprehensible terms to provide an insight into the Foundation's work and the research teams that receive funding.

The Administrative Board met again in October in order to discuss the applications for the position of Scientific Advisor; a decision was taken as to which applicants should be called in



for interviews. Candidates for the position each gave a presentation at the Administrative Board's December meeting and a decision was taken. Dr. Franz P. Gruber, who has been a member of the Board, and Prof. Peter Maier, the retiring Scientific Advisor, were warmly thanked for their hard work and commitment on behalf of the Foundation. Any other business included a discussion of the year's activities with the members of the Evaluation Committee, the 25<sup>th</sup> anniversary workshop and the talks with representatives of the SNF, which unfortunately proved unfruitful. The evening ended with a dinner.

The Strategy Committee set up by the Administrative Board held various meetings at which it drew up proposals for the Foundation's future activities.

The Administrator was busier than usual during 2012 with five meetings and preparations for changes in personnel. The Administrator deals with all matters concerning the Foundation that cannot be passed on to anyone else. In particular, he prepares all the necessary information for the Administrative Board to take their decisions, as well as dealing with correspondence with applicants and project managers. He also deals with payments, book-keeping, closing the books at the end of the financial year and the budget. In addition, he prepares the Annual Report as well as texts for the Foundation's website.

Under the chairmanship of the Scientific Advisor, the Evaluation Committee held two meetings during the year, where in particular they examined 13 new applications for funding of which they chose 6 likely projects; finally 4 were approved. In addition they examined the final reports on 4 completed projects and submitted them to the Administrative Board. We should like to take this opportunity to thank the members of the Evaluation Committee for their voluntary work in this connection.

The Scientific Advisor's tasks included publishing the 3R Info Bulletins (in the form of brochures and on the Foundation's website at [www.forschung3r.ch](http://www.forschung3r.ch)), writing the brief scientific reports in English which present the projects re-

ceiving funding on the Foundation's website and regularly updating these reports. He was also kept busy – as always – advising applicants and project managers, obtaining intermediate reports, evaluating project outlines, dealing with enquiries and explaining why projects had been rejected. Finally, he represented the Foundation at several scientific meetings in Switzerland and abroad, namely at the 1st European Conference on Replacement, Reduction and Refinement of Animal Experiments in Ecotoxicology at the EAWAG in Dübendorf. Within the context of the European Partnership for Alternative Approaches to Animal Testing (EPAA), the Scientific Advisor, being a member of the Mirror Group and the Scientific Advisory Committee, played a consulting role in relation to this European initiative.

Furthermore, in 2012 much of the Scientific Advisor's time was spent preparing and organising, together with the Swiss Laboratory Animal Science Association, the Foundation's 25<sup>th</sup> anniversary workshop, which was held on 19 and 20 November at the Technopark in Zurich. The Administrative Board would like to thank him most warmly for all his work in this connection; the participants were also immensely appreciative of the excellent programme and the impeccable organisation of the meeting.

## **25<sup>th</sup> anniversary meeting of the 3R Research Foundation and the Swiss Laboratory Animal Science Association (SGV)**

The workshop was held on 19 and 20 November 2012 at the Technopark in Zurich. There were over 400 participants, of which some 100 attended the 3R sessions. During the 5 sessions, 22 speakers from Switzerland and abroad described the many possible 3R-relevant methods that can be used in various fields. The Swiss Toxicology Association held one session in which they presented 3R-relevant progress in the field of toxicology. Representatives of the European Consensus Platform for 3R Alternatives (ecopa) from eight European countries provided information about where and what kind of 3R-relevant research was being funded and what issues were being discussed at present by the various EU committees. Short presentations were used to explain the different opportunities of consensus (interaction and sponsoring) between the 4 partners (the state, scientific circles, animal protection organisations and industry) in Europe.

The 111 pages of the Proceedings include general information about the meeting and the welcome addresses given by the Chairwoman of the 3R Research Foundation and the President of the SGV, and were handed over to all the participants. The main body of the Proceedings, however, comprises the 30 papers presented and summaries of the 18 on-going projects funded by the Foundation. The presentations included a total of over 130 images. The Proceedings and press releases about the workshop can be consulted on the Foundation's website.

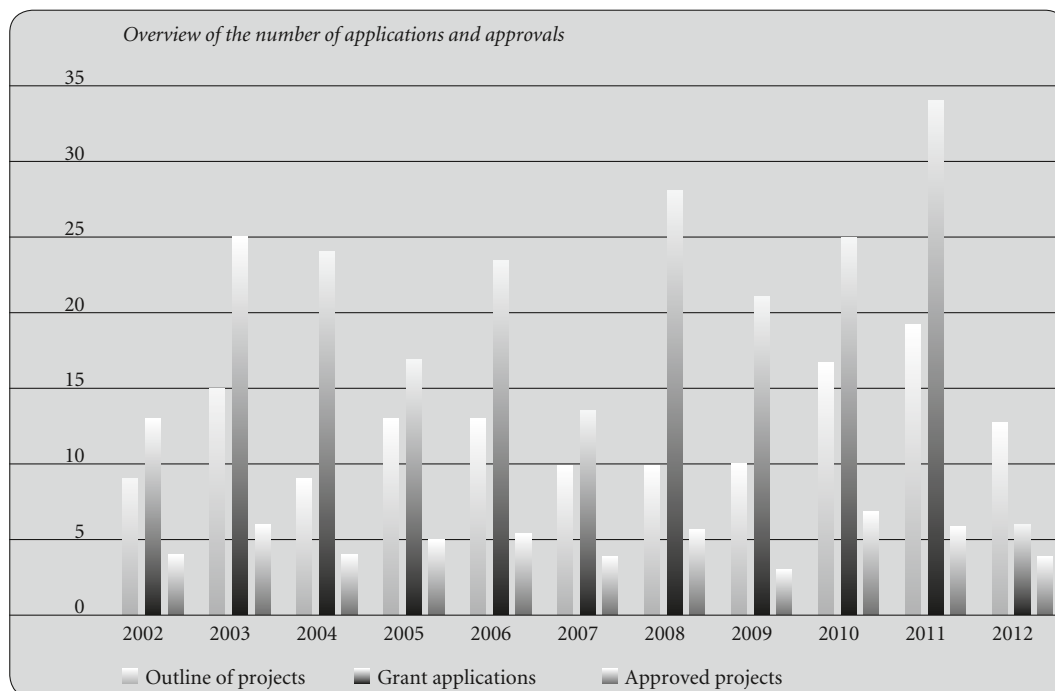
At the dinner held at the Hotel St. Gotthard in Zurich, Prof. Peter Maier, who organised the event, welcomed the 53 diners, in particular the speakers, representatives of the Federal Veterinary Office and Interpharma, and current and former members of the Administrative Board and the Evaluation Committee. In a short speech he described the Foundation's activities over the past 25 years. His hard work, which resulted in an extremely successful event, is much appreciated.

## **Personnel**

Prof. Simon P. Hoerstrup, head of the Swiss Centre for Regenerative Medicine at Zurich University Hospital and the University of Zurich, was elected to the Evaluation Committee.

As the representative of the animal protection lobby, Dr. Franz P. Gruber resigned from the Administrative Board having reached the age limit of 70 and was warmly thanked for all his work on behalf of the Foundation. Since joining the Board in 1995, Dr. Gruber had constantly brought the animal protection point of view to bear among the Board members and, with his comprehensive knowledge of research activities in relation to the 3R principles, often provided valuable impulses for the decisions that were taken. The Administrative Board greatly appreciated his willingness and his unflagging commitment. He was replaced in May 2013 by Claudia Mertens, a biologist who works with the Zurich Animal Protection League and is now the representative of this field on the Board.

At the end of the year, Prof. Peter Maier resigned as the Foundation's Scientific Advisor. He was also thanked most sincerely for all the work he had done over the past 12 years and for establishing a scientifically solid and recognised funding system through the 3R Foundation. Prof. Ernst B. Hunziker from the University of Berne has been appointed as the new Scientific Advisor and head of the Evaluation Committee.



### Overview of the number of applications and approvals

During 2012 four projects were completed (115/09, 120/10, 121/10 and 123/10). Together with those projects completed earlier, this brings the total of finished projects to 117 out of 134.

The bar-chart shows that the number of project outlines and applications increased considerably up to 2011. In contrast, the number of projects approved has remained more or less unchanged, owing to the Foundation's financial limitations. In 2012, in view of the limited funds available, the call for projects was restricted to one deadline only, namely in February 2012, and a new two-stage application procedure was introduced. Initially, applicants submit a project proposal, 13 such proposals being received in 2012. After the proposals have been examined by the Evaluation Committee, the latter then asks those whose proposed projects are relevant to the 3R principles to draw up detailed applications, 6 such detailed descriptions being submitted in 2012. Insofar as there was only one deadline for submitting proposals, which then underwent a preliminary triage by the Evaluation Committee, the figures for 2012 concerning proposals and full applications cannot be compared with figures for previous years.

### Auditors' report to the Administrative Board

Waber Treuhand GmbH in Einigen audited the financial statements for the year according to standards of limited auditing and did not find any indication that the accounts and statements do not correspond to current legislation or the principles and regulations of the Foundation.

## Financial business

A total of some CHF 676,848.25 was paid out for research in 2012. Operational expenditure for 2012 amounted to CHF 242,919.51 (project monitoring and information CHF 107,417.44, administrative costs including office infrastructure CHF 135,502.07). The increase in operational expenditure was mainly due to the activities surrounding the Foundation's 25<sup>th</sup> anniversary and for the appointment of the new Scientific Advisor. Total expenditure therefore amounted to CHF 919,767.76.

On the income side, the equal financial commitment of the federal authorities and Interpharma represented the basic funding for the Foundation's activities, each providing in 2012 an amount of CHF 485,000. This annual contribution was higher than usual and helped to alleviate the Foundation's financial problems somewhat. In addition they made a one-time supplementary contribution of CHF 50,000 for the Schindler Assessment Project. A further income item of CHF 23,109.86 resulted from financial income and repayment of unused project funding.

Total income was therefore CHF 1,043,109.86 while total expenditure amounted to CHF 919,767.76, giving an excess of income over expenditure of CHF 123,342.10. The unused funds item consequently rose by CHF 164,528.86 to

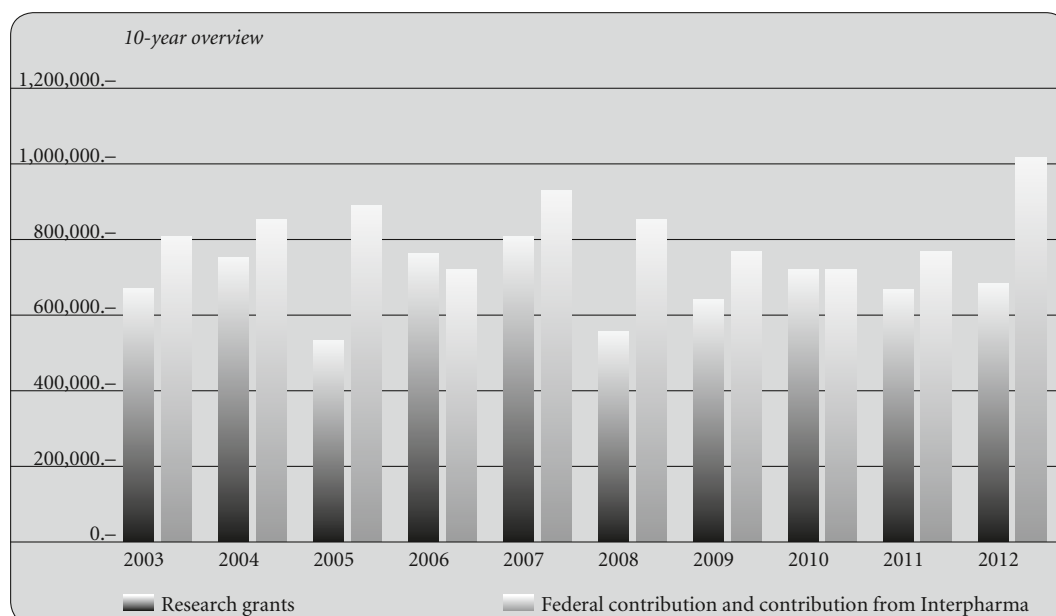
CHF 287,870.96 by the end of 2012, the latter figure constituting the Foundation's new reserve of liquid assets.

At the end of 2012 the total earmarked for projects approved by the Board but not yet paid out amounted to CHF 844,157.15. This future liability is covered by Interpharma's promise of funding (V) together with the contribution from the Confederation. The Foundation's credit with Interpharma amounted to CHF 712,000 at the end of 2012.

The budget for 2013 includes CHF 603,534.15 for current projects and a maximum amount of CHF 500,000 for new projects.

## Overview of grants awarded between 1987 and 2012

At the end of 2012 a total of CHF 18,289,696.45 had been granted for projects and other subsidies, of which CHF 17,445,539.30 had been paid out so far. Together the federal authorities and Interpharma have contributed CHF 20,966,000 to the Foundation since 1987.



**Financial statements**

<i>Profit and loss account 2012</i>	<i>Expenditure</i>	<i>Income</i>
<i>Income</i>		
Federal contribution		495,000.00
Contribution from Interpharma		525,000.00
Total contributions		1,020,000.00
Capital yield		409.60
Reimbursement of research grants		22,288.76
Other income		511.50
Total income		1,043,109.86
<i>Expenditure</i>		
Research grants	676,848.25	
Project supervision and information	107,417.44	
Administrative expenses	135,502.07	
Total expenditure	919,767.76	
Excess income over expenditure	123,342.10	
	1,043,109.86	
<i>Balance as per 31<sup>st</sup> December 2012</i>		
<i>Liquid Assets</i>		
Bank	195,032.36	
Accounts payable	354.50	
Accounting apportionment assets	124,044.00	
<i>Liabilities</i>		
Accounting apportionment liabilities		30,559.90
Unused research funds		
– Carried forward 1. 1. 2012	164,528.86	
– Excess income over expenditure	123,342.10	287,870.96
Capital of the Foundation		1,000.00
	319,430.86	319,430.86

**Contingent liabilities**

Approved research grants not yet paid out CHF 844,157.15.

Münsingen, 15 March 2013

3R RESEARCH FOUNDATION

*Chairwoman*

signed C. Egerszegi

*Administrator*

signed E. Diener

**3R Info Bulletins**

In 2012 three more new 3R Info Bulletins (ISSN 1421-6590) were published in English and distributed to some 1,000 interested parties. The information bulletins are also published on the Foundation's website ([www.forschung3r.ch/en/publications/index.html](http://www.forschung3r.ch/en/publications/index.html)), as well as in pdf format.

**The latest 3R-INFO-BULLETINS are:**

*N° 50, December 2012*

Still relevant twenty-five years on; 25 years of Funding the 3Rs – past accomplishments and future prospects

*N° 49, June 2012*

Bacterial Meningitis: Investigating Injury and Regenerative Therapy in vitro

*N° 48, February 2012*

A novel ex vivo mouse aorta perfusion model

**List of the other 3R-INFO-BULLETINS**

*N° 1, June 1994*

Foundation Research 3R

*N° 2, September 1994*

mAbs without mice?

*N° 3, December 1994*

Prof. Gerhard Zbinden and 3R

*N° 4, April 1995*

Predicting human drug metabolism

*N° 5, August 1995*

Human recombinant antibodies

*N° 6, September 1995*

Call for 3R research proposals

*N° 7, March 1996*

The three 'R's of Russell and Burch, 1959

*N° 8, August 1996*

Regulation of digestion in cell culture

*N° 9, October 1996*

Permanent fish cell cultures as novel tools in environmental toxicology

*N° 10, August 1997*

10 years 3R Research Foundation

*N° 11, March 1999*

Immunization of laboratory animals

*N° 12, September 1999*

Leishmaniasis: development of an in vitro assay for drug screening

*N° 13, January 2000*

Identification of neurotoxic chemicals in cell cultures

*N° 14, May 2000*

Transgenic protozoa as an alternative to transgenic animals

*N° 15, September 2000*

Aggregating brain cell cultures: Investigation of stroke related brain damage

*N° 16, January 2001*

Housing and husbandry conditions affect stereotypic behaviour in laboratory gerbils

*N° 17, May 2001*

Fever in the test tube – towards a human(e) pyrogen test

*N° 18, September 2001*

Prevention of adverse effects in pigs after vaccination

*N° 19, January 2002*

Phenotype characterisation and welfare assessment of transgenic mice

*N° 20, May 2002*

Animal-free screening of biological materials for contamination by rodent viruses

*N° 21, September 2002*

Identification of new human skin irritation markers for tests with human skin reconstructs

*N° 22, January 2003*

Environmental enrichment does not affect the variability of animal experimentation data in the Light/Dark test

*N° 23, May 2003*

Simulation of stroke related damage in cultured human nerve cells

*N° 24, September 2003*

Generation of parasite cysts in cultured cells instead of living animals

*N° 25, January 2004*

Formation of new blood vessels in the heart can be studied in cell cultures

*N° 26, May 2004*

Immune cells in the liver: The generation and use of a mouse Kupffer cell line

*N° 27, September 2005*

The tick blood meal: From a living animal or from a silicone membrane?

- N<sup>o</sup> 28, January 2005  
Bone metabolism and bone-biomaterial interactions can be studied ex vivo
- N<sup>o</sup> 29, May 2005  
Computer-based quantification of (adverse) effects triggered by drugs and chemicals
- N<sup>o</sup> 30, September 2005  
Environmental enrichment does not disrupt standardization
- N<sup>o</sup> 31, January 2006  
Improvement of Pain Therapy in Laboratory Mice
- N<sup>o</sup> 32, May 06  
Non-Invasive Methods: Investigation of Airways Diseases by MRI in Rats
- N<sup>o</sup> 33, September 06  
Predicting drug hypersensitivity by in vitro tests
- N<sup>o</sup> 34, January 07  
Exploring natural anticoagulation by endothelial cells: A novel in vitro model
- N<sup>o</sup> 35, May 07  
From blood to brain and vice versa: Transport Processes in Choroid Plexus can be studied in vitro
- N<sup>o</sup> 36, January 08  
Host pathogen interactions can be studied in amoebae instead of laboratory animals
- N<sup>o</sup> 37, June 08  
The bioconcentration of chemical substances in fish can be determined in vitro
- N<sup>o</sup> 38, October 08  
An in-vitro system for detecting the health effects of inhaled particles and gases
- N<sup>o</sup> 39, February 2009  
Detection of Pain in Laboratory Animals via Gene Expression?
- N<sup>o</sup> 40, June 2009  
Refined ex-vivo rodent heart model reduces in vivo experimentation
- N<sup>o</sup> 41, October 2009  
A novel in-vitro cell model of the human airway epithelium
- N<sup>o</sup> 42, February 2010  
The blood-brain barrier in a dish: a new multicellular in vitro model
- N<sup>o</sup> 43, June 2010  
Fish, Acute Toxicity Test: The number of animals can be reduced
- N<sup>o</sup> 44, October 2010  
From pigs to cells: Virulence of classical swine fever virus is predictable in cell cultures
- N<sup>o</sup> 45, February 2011  
Serum-free defined media, a largely unsolved problem in cell culture
- N<sup>o</sup> 46, May 2011  
Toxoplasma gondii virulence is predictable in cultured human cells
- N<sup>o</sup> 47, October 2011  
Metabolism as part of alternative testing strategies in fish

**List of Projects**

A complete list of projects with summaries of each can be found on the Foundation's website ([www.forschung3r.ch/en/projects/index.html](http://www.forschung3r.ch/en/projects/index.html)).

The brief scientific project reports in English, which are updated once a year, indicate that almost all projects have progressed well. This platform for presenting research work enables research teams worldwide to find out about new 3R methods very quickly.

**List of new projects approved in 2012**

- 134/12 Prof. Stijn Vandenberghe  
ARTORG Center for Biomedical Research,  
University of Berne, Switzerland  
*Development of a cardiovascular simulator  
with autoregulation*
- 133/12 Prof. Robert Rieben  
Department of Clinical Research,  
University of Berne, Switzerland  
*Development of an in vitro system to grow  
and investigate vascular endothelial cells  
under physiological flow*
- 132/12 Prof. Matthias P. Lutolf  
Institute of Bioengineering, EPFL, Swiss  
Federal Institute of Technology Lausanne,  
Switzerland  
*Identification of predictive in vitro markers  
for hematopoietic stem cell function*
- 131/12 Prof. Christian Heinis  
Laboratory of Therapeutic Peptides and  
Proteins, EPFL, Swiss Federal Institute of  
Technology Lausanne, Switzerland  
*Antibody phage selection strategy for ap-  
plication in non-specialized laboratories*

**List of current projects and those completed in 2011 and 2012**

- 82/02 Dr. Nicolau Beckmann  
Novartis Institute of Biomedical Research,  
Basle  
*Magnetic resonance imaging (MRI) for the  
non-invasive assessment of lung inflamma-  
tion and pulmonary function in the rat*  
Completed in 2011
- 99/05 Prof. Pierre Cosson  
Medical Faculty, University Medical Cen-  
tre, Geneva  
*Non-mammalian Experimental Models for  
the study of bacterial infections (NEMO net-  
work)*  
Completed in 2011
- 101/06 Prof. Norbert Goebels  
Dept. of Neurology and Neuroimmuno-  
logy, University Hospital Zurich  
*Organotypic CNS slice cultures as an in-  
vitro model for immune mediated tissue  
damage and repair in multiple sclerosis*  
Completed in 2011
- 103/06 Prof. Stephen Leib  
Institute of Infectious Diseases,  
University of Berne  
*An in vitro Model of Central Nervous Sys-  
tem Infection and Regeneration: Neuronal  
Stem Cells as Targets of Brain Damage and  
Regenerative Therapies in Bacterial Menin-  
gitis*  
Completed in 2011
- 107/07 Dr. Sushila D'Souza  
Pasteur Institute of Brussels  
*Evaluation of an in vitro model to identify  
host parameters associated with virulence of  
Toxoplasma gondii strains*  
Completed in 2011
- 108/07 Prof. Helmut Segner  
Center for Fish and Wildlife Health,  
University of Berne  
*In vitro fish hepatocytes as source of metabo-  
lic clearance data in alternative approaches  
for the reduction or replacement of in vivo  
bioaccumulation testing with fish*  
Completed in 2011



- 109/08 Prof. Paul Honegger and Dr. Marie-Gabriele Zurich  
 University of Lausanne  
*Evaluation of lipid fractions for the substitution of serum in cell culture media*  
 Completed in 2011
- 110/08 Prof. Jennifer Keiser  
 Swiss Tropical and Public Health Institute, Basle  
*Development of an in vitro assay for the screening of antischistosomal drugs*  
 Completed in 2011
- 111/08 Prof. Patrick Hunziker  
 University Hospital, Basle  
*Establishment of an organ ex-vivo tissue slice model for cardiovascular research in particular for therapeutic atherosclerosis targeting*  
 Completed in 2011
- 112/08 Dr. Zhijie Luo and Prof. Jennifer Kirkham  
 Leeds Dental Institute, University of Leeds, UK  
*A novel in vitro model for holistic assessment and optimisation of engineered tissue for functional cartilage repair*  
 Completed in 2011
- 113/08 Dr. Artur Summerfield/Dr. Kenneth McCullough  
 Institute of Virology and Immunoprophylaxis (IVI), Mittelhäusern  
*Generic in vitro evaluation assay for immunological correlates of protection to replace animal challenge infections*
- 114/08 Dr. Hans Ruffli  
 ecotoxsolutions, Basle  
*Reduction in the number of fish used in the fish acute toxicity test*  
 Completed in 2011
- 115/09 Dr. Olivier Preynat-Seauve  
 Department of Pathology and Immunology, University of Geneva  
*Engineering of a human brain tumor model to replace animal experimentation*  
 Completed in 2012
- 116/09 Dr. Anna Oevermann  
 Neurocenter, DCR-VPH, Vetsuisse Faculty, University of Berne  
*Organotypic slice cultures derived from brains obtained from slaughterhouses as an in vitro alternative for the investigation of neuroinfectious diseases in ruminants*
- 117/09 Prof. Maria Wartenberg  
 Workgroup for Molecular Cardiology, Friedrich-Schiller University, Jena  
*Development of an in vitro model from embryonic stem cells for identifying tissue inflammation as a reaction to implanted material (INFPLANT)*
- 118/10 Dr. Dalu Mancama  
 CSIR, Biosciences Division, Pretoria, South Africa  
*Engineering of an in vitro hepatocyte tissue system for malaria liver infection research*
- 119/10 Dr. Sara Gonzalez Andino  
 Department of Clinical Neurosciences, University of Geneva  
*Non-invasive electrical monitoring of the population spiking activity in the central nervous system*
- 120/10 Prof. Denis Jabaudon  
 Department of Basic Neurosciences, University of Geneva  
*Development of non-invasive strategies to study spinal cord disease, injury and repair*  
 Completed in 2012
- 121/10 Prof. Roman Chrast and Prof. Josef Kapfhammer  
 Department of Medical Genetics, University of Lausanne, and Anatomical Institute, University of Basle  
*A new in vitro model to study therapeutic approaches to improve spinal cord regeneration and repair after injury*  
 Completed in 2012

- 122/10 Dr. Helene Rohrbach  
Department of Clinical Veterinary  
Medicine, University of Berne  
*Improved perioperative analgesia and re-  
duced stress during recovery for the experi-  
mental animal: ultrasound-guided sciatic  
and femoral nerve block in sheep and quan-  
titative assessment of block quality*
- 123/10 Dr. Hans Rufli  
ecotoxsolutions, Basle  
*Use of “moribund“ stage in the fish acute  
toxicity test according to OECD guideline  
203 and its effect on LC50 values*  
Completed in 2012
- 124/10 Dr. Martin Clauss  
Orthopaedics Department,  
Cantonal Hospital Liestal  
*Comparative in vitro and in vivo testing  
on biofilm formation on the surface of bone  
grafts*
- 125/11 Dr. Oliver G. Weingart  
Institute of Food Sciences, Nutrition and  
Health, Zurich Federal Institute of Tech-  
nology, Switzerland  
*Nerve-cell mimicking liposomes as an in  
vitro alternative for demonstrating the po-  
tency of toxins with multistep pathways such  
as Botulinum neurotoxins (BoNT)*
- 126/11 Dr. Charaf Benarafa  
Theodor Kocher Institute, University of  
Berne, Switzerland  
*Model development and validation to in-  
vestigate myeloid cell homeostasis*
- 127/11 Prof. Thomas Kaufmann  
Institute of Pharmacology, University of  
Berne, Switzerland  
*Establishing A Novel System For Quanti-  
tative Production of Murine Basophils In  
Vitro*
- 128/11 Dr. Volker Thiel  
Institute of Immunobiology, Cantonal  
Hospital St. Gallen, Switzerland  
*Genetic modification of the human airway  
epithelium – a paradigmatic system to study  
host responses to human respiratory virus-  
es*
- 129/11 Prof. Zhigang He  
Children’s Hospital, Boston, USA  
*Using microfluidic chamber to study mito-  
chondrial transport in PTEN and SOCS3  
dependent axonal regeneration*
- 130/11 Prof. Ernst B. Hunziker  
Center of Regenerative Medicine for Skel-  
etal Tissues, University of Berne, Switzer-  
land  
*Establishment of an in-vitro organ-slice de-  
fect model for meniscal repair in orthopaedic  
research*





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