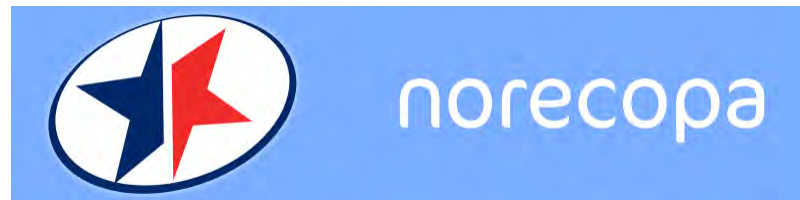


## Where can we find 3R literature?

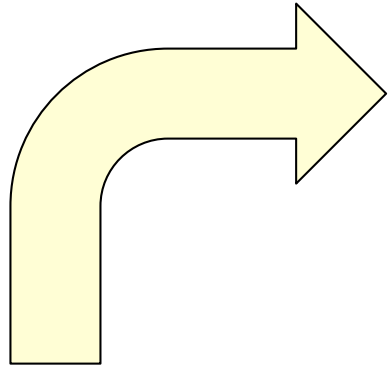
Adrian Smith

*adrian.smith@norecopa.no*

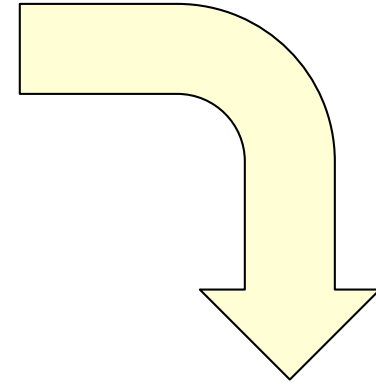


*www.norecopa.no*

- What is 3R literature?
- Why is it hard to find?
- What can we do about?
- Examples of 3R sources
- Tools for searching the literature

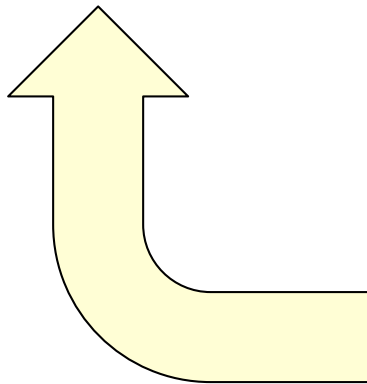


Literature  
search

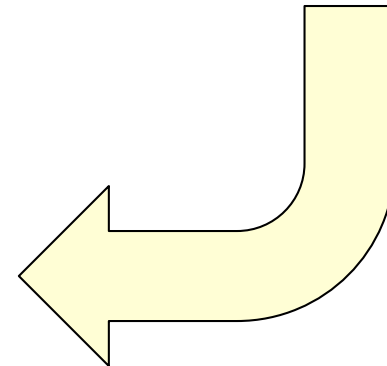


Reporting

Planning



Research



# *3R literature embraces all 3R alternatives*

## **1) Replacement alternatives**

3D models

Audiovisual aids

Computer simulations

Mannekins, simulators, robots

QSAR (Quantitative Analysis of Structure/Activity Relationships)

Cell and tissue cultures, organoids, organ perfusion

High Throughput Screening (HTS), organs-on-a-chip

Biochemical & immunological methods (RIA, ELISA)

Hybrid DNA technique, GMM

Trials on “lower” organisms

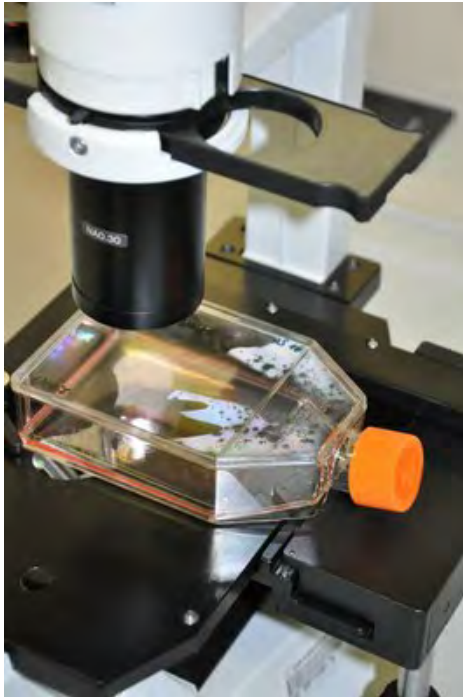
Acute experiments (terminal anaesthesia)

Trials on dead animals

Trials on humans (microdosing and medical imaging)

Synthesis of new evidence from experiments that have already been performed

# High Throughput Screening (HTS)



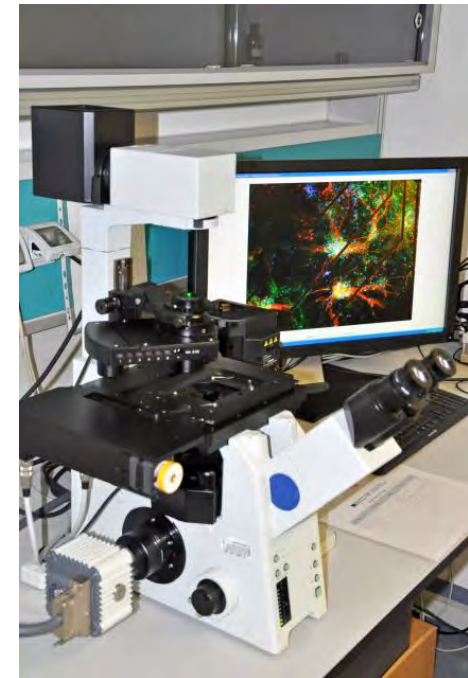
Cell culture and  
compound management



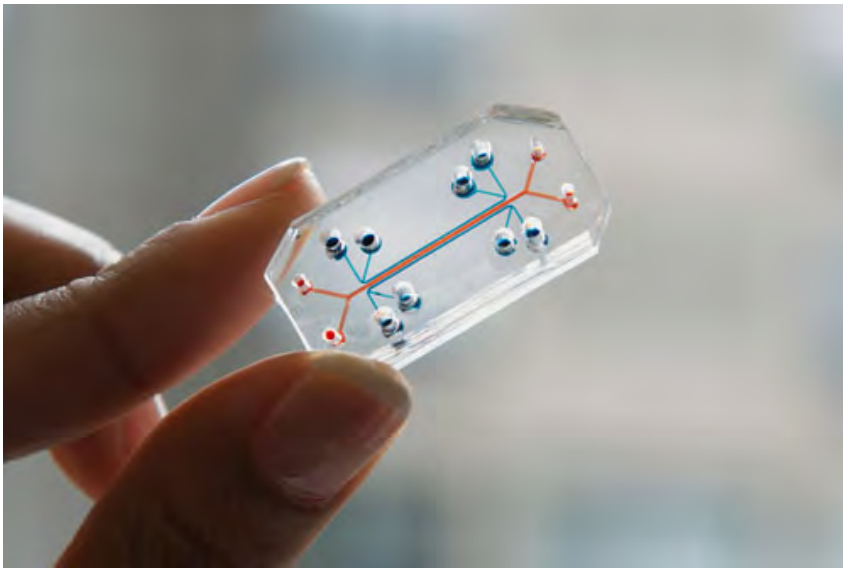
Robotic platform with high-throughput  
liquid handler for sample dilution  
and treatment.

Optical plate reader and incubator

Data management system

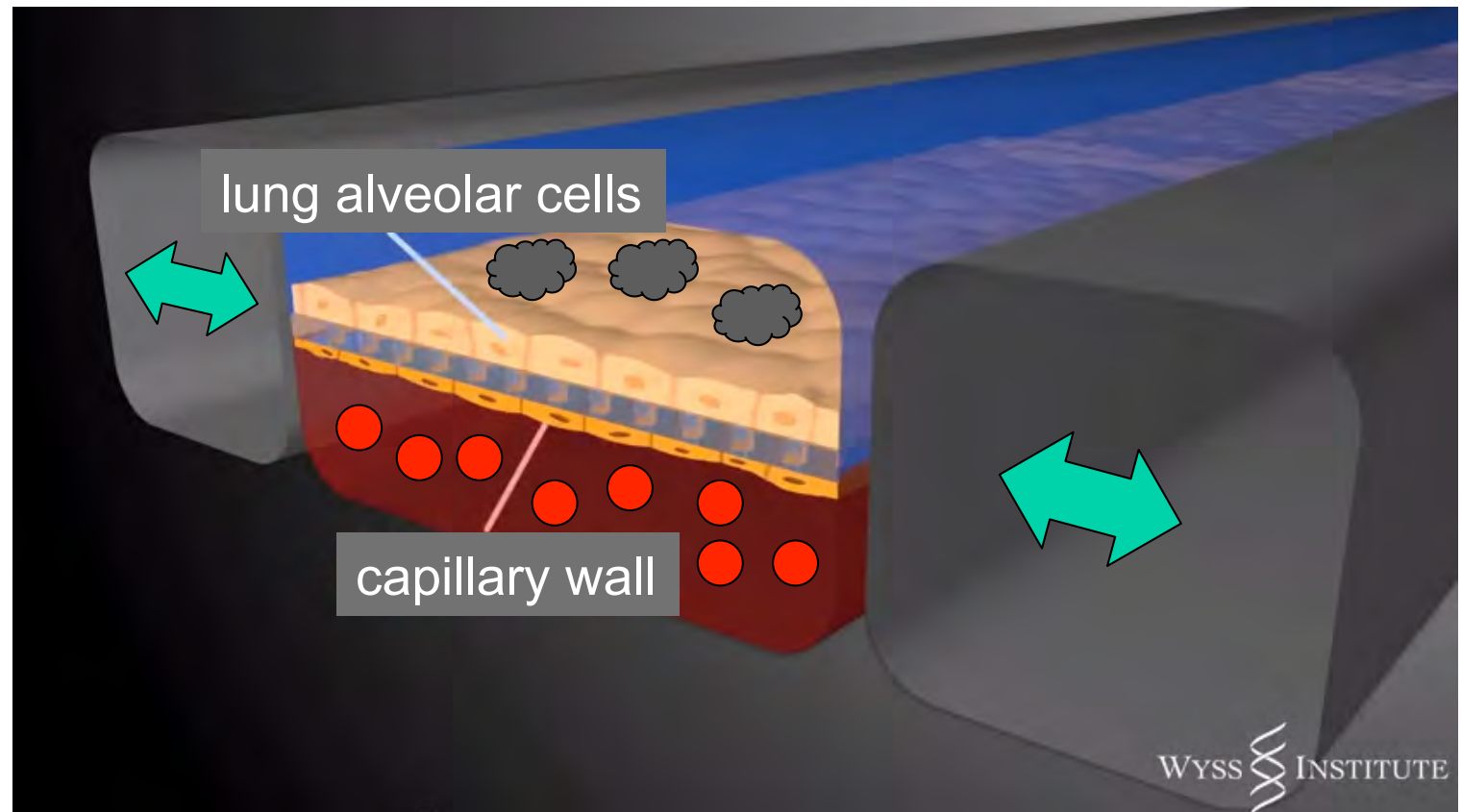


Automated **imaging**  
microscope for **high-**  
**content screening**



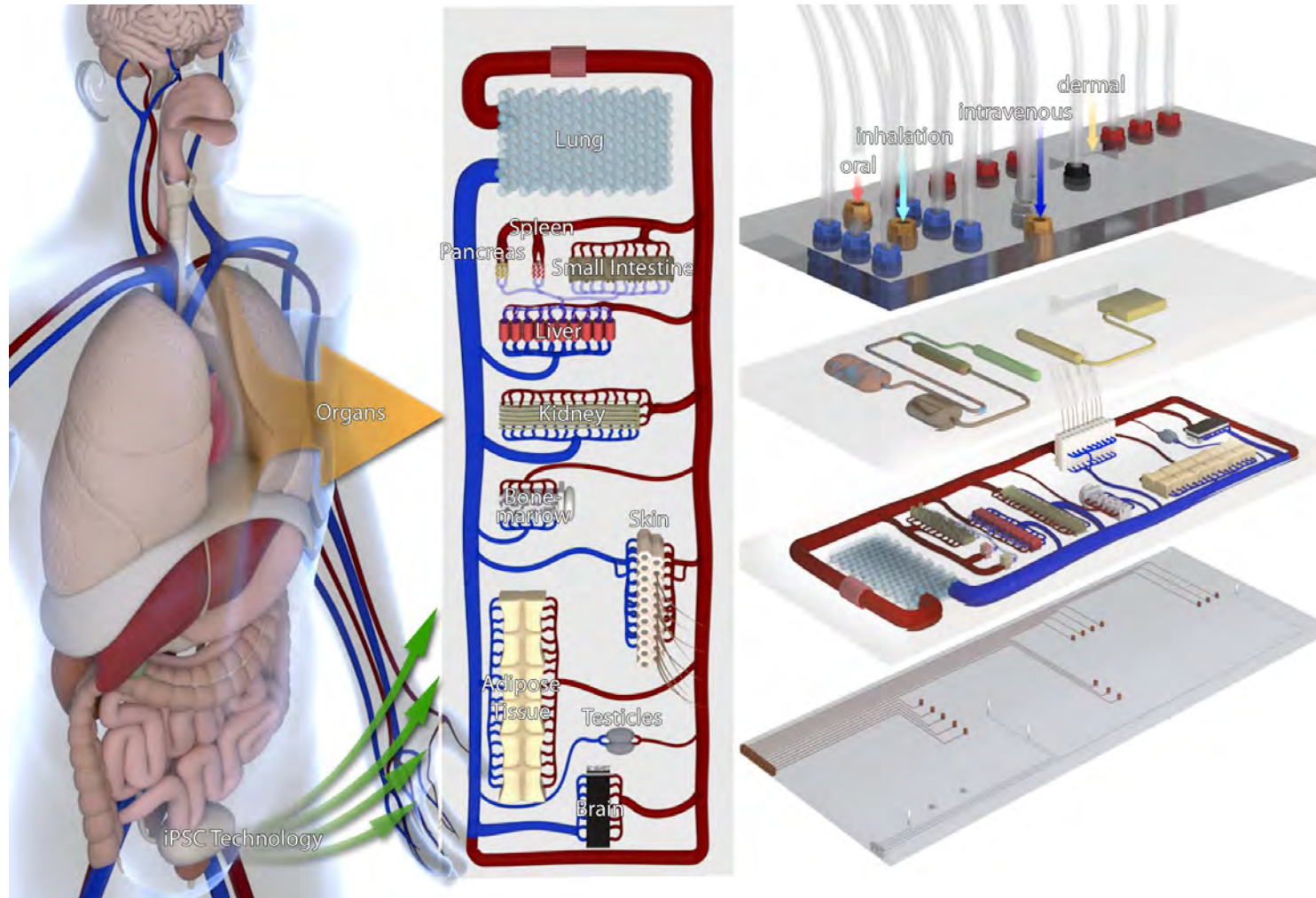
# Lung-on-a-chip

Wyss Institute, Harvard





# Next generation Multi-Organ-Chip



Marx et al., Altern Lab Anim. 2012 Oct;40(5):235-57

- Norecopa -

# ***Integrating natural science and technology: Fish and fish robots***



photo: Norecopa

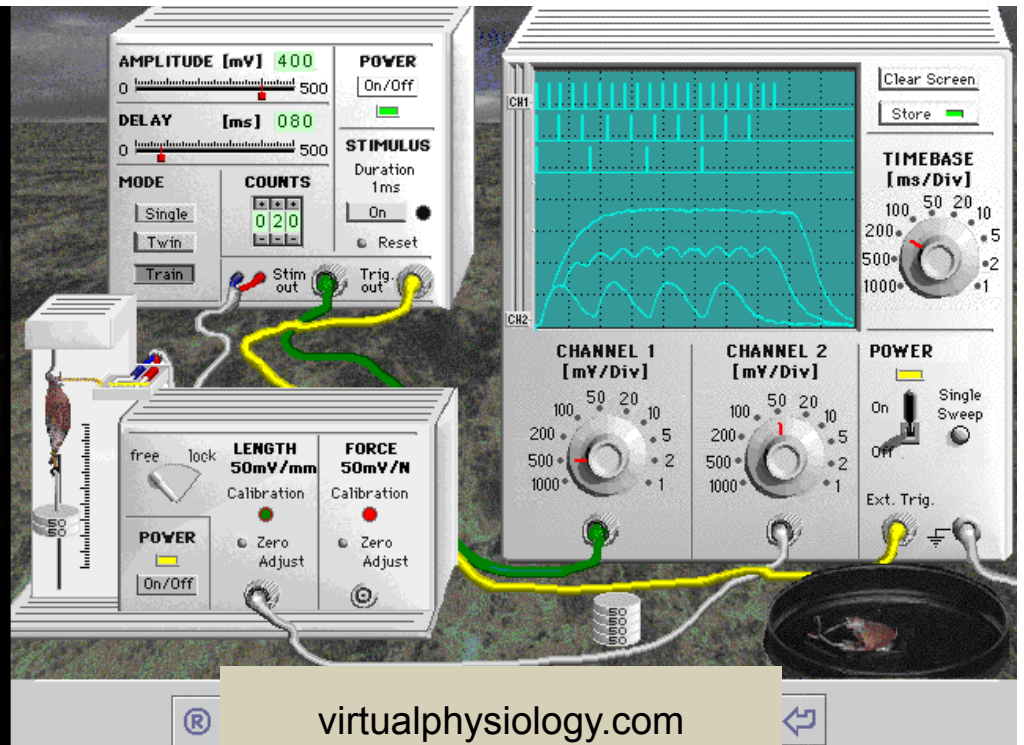


***Prof. Maarja Kruusma***





3dglasshorse.com



virtualphysiology.com



rescuecritters.com



limbsandthings.com



Rats from IKEA





Photo: Joe Mcdonald/ Corbis

<http://www.theguardian.com/commentisfree/2012/mar/14/laboratories-animals-anti-vivisection-campaign>

**Fidelity:** overall proportionate difference (e.g. HiFi)

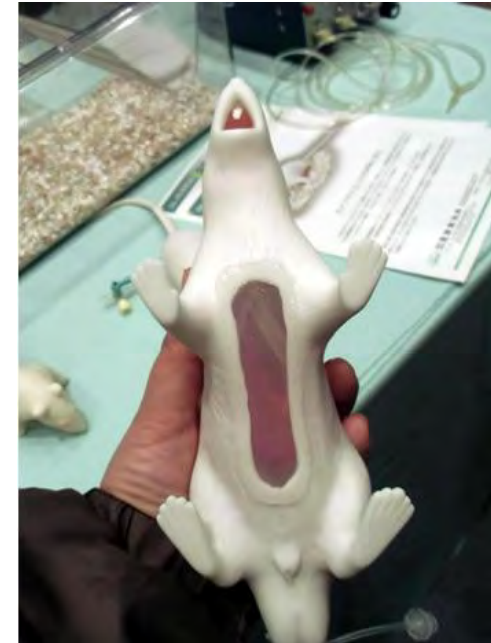
**Discrimination:** the extent to which the model reproduces one particular property in which we are interested



[www.frame.org.uk/tag/russell-and-burch](http://www.frame.org.uk/tag/russell-and-burch)



[https://www.wardsci.com/store/catalog/product.jsp?catalog\\_number=813015#](https://www.wardsci.com/store/catalog/product.jsp?catalog_number=813015#)



<http://www.interniche.org/ko/node/5134>

***The potential for 3R alternatives cannot be evaluated until the objective of the study is known. This applies to all use of animals in research, testing, education and training***

*Possible objectives in education & training:*

- Teaching and practising:
  - laboratory skills
  - general animal handling skills
  - preparation-specific animal skills
- imparting good ethical thinking
- new knowledge and reinforcing existing
- data handling skills
- experimental design skills
- communication skills (oral, written)
- groupwork
- staff-student interaction

*AJ Smith & K Smith, 2004*

*Guidelines for humane education:  
Alternatives to the use of animals in  
teaching and training*

Proceedings of the 4th World Congress on Alternatives and Animal Use in the Life Sciences, New Orleans, August 2002.

[http://www.atla.org.uk/wp-content/plugins/s2member-files/  
32\\_S1a\\_3\\_Plenary\\_specialcontribution.pdf](http://www.atla.org.uk/wp-content/plugins/s2member-files/32_S1a_3_Plenary_specialcontribution.pdf)  
(log-in required, pages 16-26)



# ***Where do I find information about alternatives for use in Education and Training?***

## Databases

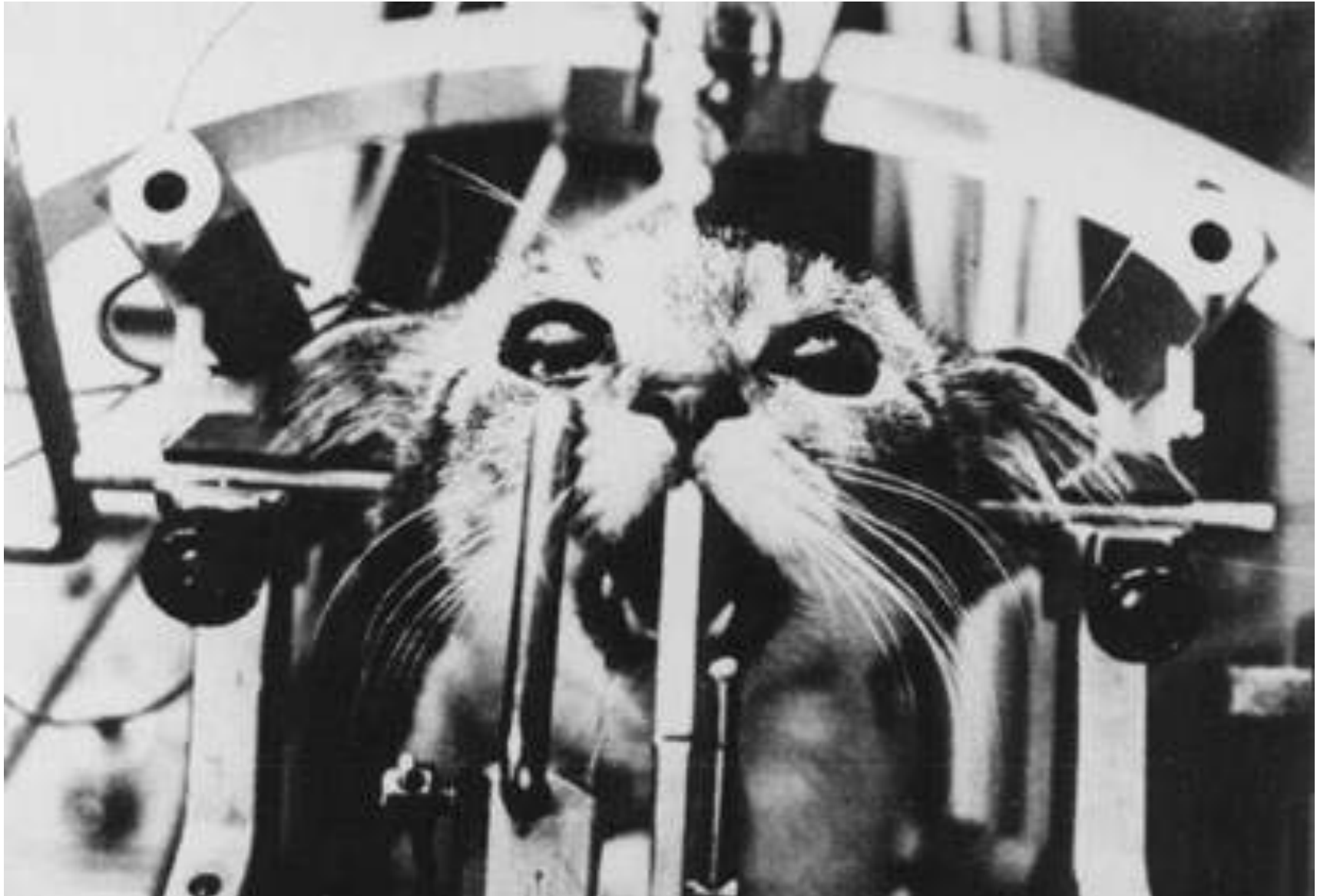
NORINA ([oslovet.norecopa.no/NORINA](http://oslovet.norecopa.no/NORINA))

InterNICHE ([interniche.org/en/alternatives](http://interniche.org/en/alternatives))

## Loan system

InterNICHE ([interniche.org/en/loansystem](http://interniche.org/en/loansystem))

***Do we need an alternative?***

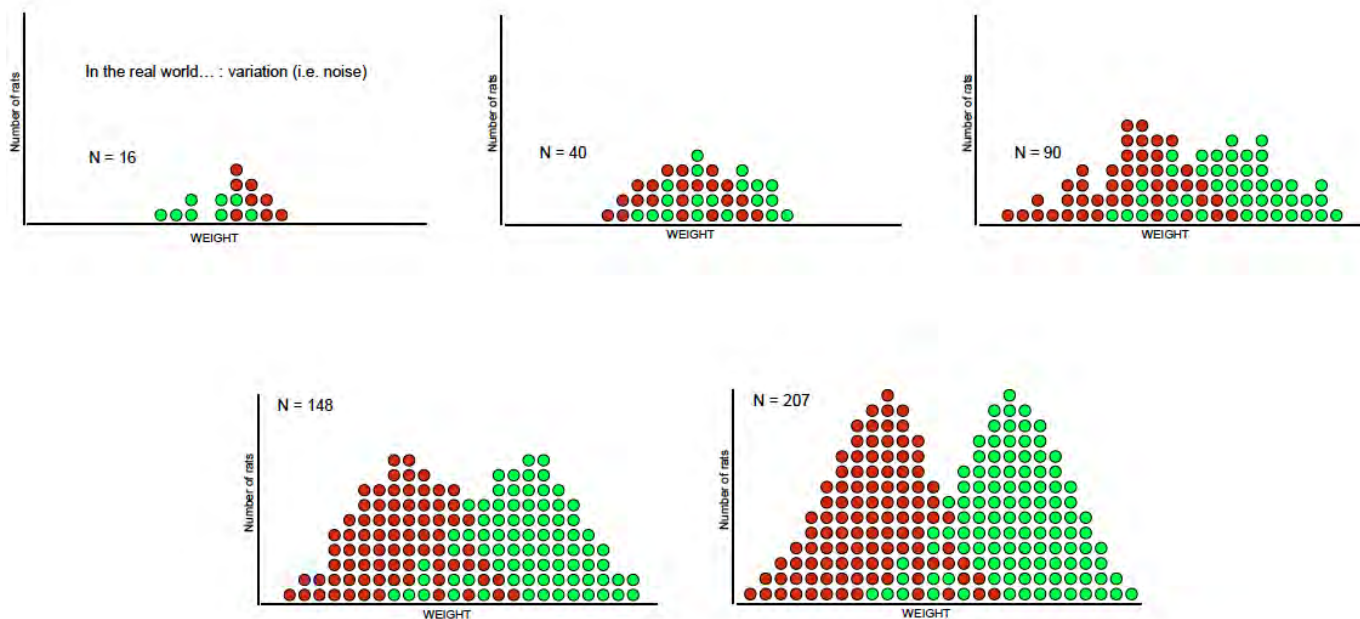


<http://www.all-creatures.org/anex/cat-res-07.html>

### 3) *Reduction alternatives*

A good statistician is the lab animal's best friend.

Combined with methods to reduce background “noise”.



## Sources of background “noise”:

- Age, sex, weight
- Stress, subclinical disease
- Room temperature, animal cage
- Environmental “enrichment”
- Temporal differences between treatments
- Climatic factors
- Position of cage in the room
- Experimenter
- Animal Technician (weekend workers)
- and many more

### ***3) Refinement alternatives***

*“Simple” techniques?*



Photo: NMBU

*Are they feasible? e.g. i.m. injections*

*“Simple” identification methods?  
Do they affect the animal?*



Photo: T. Poppe, NMBU



[http://blogs.discovermagazine.com/notrocketscience/2011/01/12/flipper-bands-impair-penguin-survival-and-breeding-success/#.VLU6\\_8Y7\\_wo](http://blogs.discovermagazine.com/notrocketscience/2011/01/12/flipper-bands-impair-penguin-survival-and-breeding-success/#.VLU6_8Y7_wo)



Photo: colourbox.com



## Refinement to avoid **contingent suffering**

(not just direct suffering caused by the procedure)

e.g. fear, boredom, discomfort

which may be caused by

e.g. transport, housing, husbandry, social hierarchy

Single-housed male mice show symptoms of what in humans would be characterised as depression

<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0111065>



***An useful additional (but largely unknown) tool...***

Carol M. Newton (1925-2014)



National Library of Medicine

## ***The three S's***

- *Good Science*
- *Good Sense\**
- *Good Sensibilities\**

***\*We can do this ourselves without scientific literature!***

Carol M Newton, quoted in Rowsell HC (1977): The Ethics of Biomedical Experimentation in The Future of Animals, Cells, Models, and Systems in Research, Development, Education, and Testing pp. 267-281, National Academy of Sciences, Washington, D.C., ISBN 0-309-02603-2.

## Creating a culture of care

Friday 22 August 2014

*Dr Marilyn Brown, Corporate Vice President of Global Animal Welfare at the contract research organisation Charles River, has many years of experience managing experimental facilities and animal care programmes.*

<https://www.nc3rs.org.uk/news/creating-culture-care>

# ILAR JOURNAL

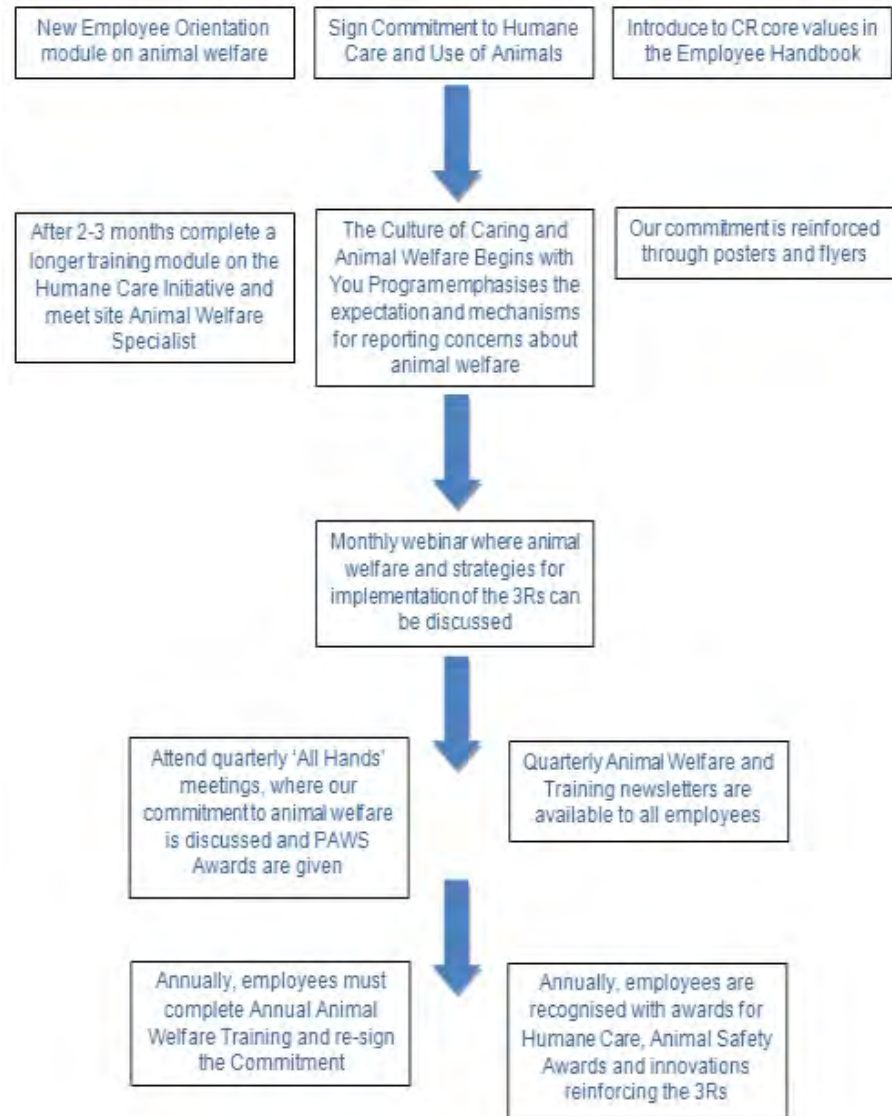
## Establishing a Culture of Care, Conscience, and Responsibility: Addressing the Improvement of Scientific Discovery and Animal Welfare Through Science-based Performance Standards

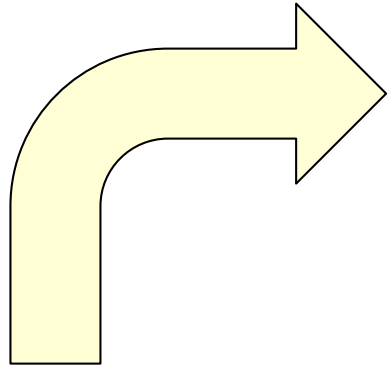
H. J. Klein and K. A. Bayne

Address correspondence and reprint requests to Dr. Klein, Merck Research Laboratories, WP42-211, West Point, PA 19486, or email [Hilton\\_klein@merck.com](mailto:Hilton_klein@merck.com).

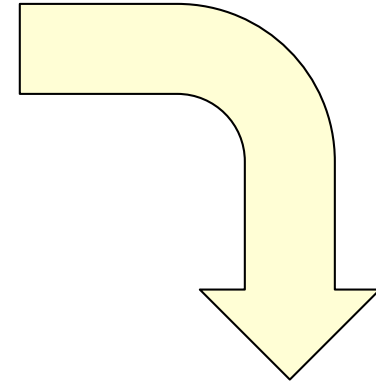
<http://ilarjournal.oxfordjournals.org/content/48/1/3.full>

### Training for new staff



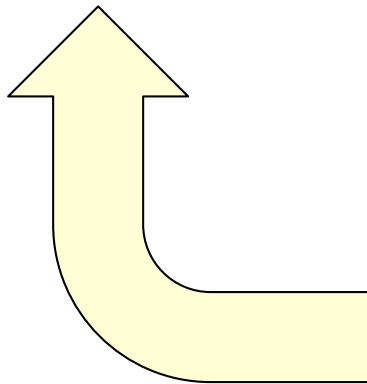


Literature  
search

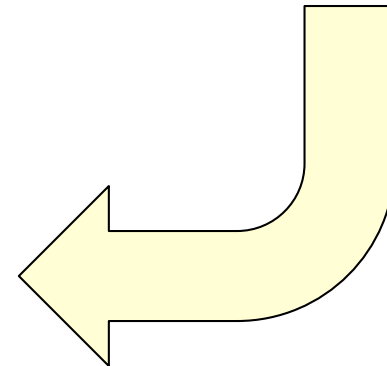


Reporting

Planning



Research



## *Why is 3R literature hard to find?*

- Bibliographic databases are often not used adequately (poor overlapping between the databases)
- Too few scientists are aware of the specialist 3R-databases
- Scientists rarely use "3R" words when they write titles/abstracts/keywords for their papers
- Databases rarely flag 3R-papers with explicit thesaurus terms ☹️
- We have no single "Journal of Alternatives"

Reporting has historically been poor:

*Jane Smith et al. (1997): 149 papers in 8 journals from 1990-1991:*

*Parameters not mentioned:*

*Number of animals: 30%*

*How the animals were killed: 45%*

<i>Sex</i>	<i>28%</i>	<i>Room temperature</i>	<i>72%</i>
<i>Age</i>	<i>52%</i>	<i>Relative humidity</i>	<i>89%</i>
<i>Weight</i>	<i>71%</i>	<i>Photoperiod</i>	<i>72%</i>
<i>Source</i>	<i>53%</i>	<i>Number of animals/cage</i>	<i>73%</i>



*Often detailed descriptions of chemicals, equipment and treatments, but very little about the animals, choice of sample size, randomisation etc:*

*‘white mice were used’*

*Many of these omissions make it harder to advance the 3Rs,  
e.g.*

- methods of drug administration and blood sampling*
- details of anaesthesia and analgesia*
- humane endpoints*

*Kilkenny C et al. (2009)*

*271 papers, mostly in 2003-2005*

*<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0007824>*

*Many studies did not*

- *describe the animals adequately*
- *describe how the sample size was chosen*
- *describe how the animals were allocated to the treatment groups, and whether the observations were performed blind.*

Even the titles, keywords and abstracts are often not very informative and lack 3R terms

**The development of Response Surface  
Pathway Design in toxicity studies**

*The development of Response Surface  
Pathway Design to reduce animal numbers in  
toxicity studies*

## 3R methods are often not highlighted in the scientific literature



[http://www.theodora.com/rodent\\_laboratory/  
blood\\_collection.html](http://www.theodora.com/rodent_laboratory/blood_collection.html)



photo:NMBU

*SCID-Hu mice immunized with a pneumococcal vaccine produce specific human antibodies and show increased resistance to infection.*

Saphenous vein puncture for  
blood sampling of the mouse, rat,  
hamster, gerbil, guinea-pig,  
ferret and mink

Visibility! Not necessarily in a high-impact journal.



## Most-Cited Articles as of May 1, 2015 -- updated monthly

Rankings based on citations to online articles from HighWire-hosted articles.

### 1. Working Party Report:

W. Nicklas, P. Baneux, R. Boot, T. Decelle, A. A. Deeny, M. Fumanelli, and B. Illgen-Wilcke

**Recommendations for the health monitoring of rodent and rabbit colonies in breeding and experimental units**

Lab Anim January 1, 2002 36: 20-42, doi:10.1258/0023677021911740

» [Full Text \(PDF\)](#)

### 2. Articles:

C. Moolenbeek and E. J. Ruitenber

**The 'Swiss roll': a simple technique for histological studies of the rodent intestine**

Lab Anim January 1, 1981 15: 57-59,  
doi:10.1258/002367781780958577

» [Abstract](#) » [Full Text \(PDF\)](#)

### 3. Papers:

Annelise Hem, Adrian J. Smith, and Per Solberg

**Saphenous vein puncture for blood sampling of the mouse, rat, hamster, gerbil, guineapig, ferret and mink**

Lab Anim October 1, 1998 32: 364-368,  
doi:10.1258/002367798780599866

» [Abstract](#) » [Full Text \(PDF\)](#)

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Laboratory Animals Ltd

Affiliated Societies

*Part of the problem:*

*Reporting (the Materials & Methods section) should ideally be so detailed that it is possible to reproduce the study in another lab.*

*But this information takes space.*



*Although space is limited, we waste space...*

*'drinking' water*

*'farm' pigs*

*'under approved conditions' (who approved them?)*

*'housed under standard conditions'*

*'given analgesia'*

*Many journals now offer supplementary online space (generally unlimited) where more information about the methods and results can be posted.*

*And most people have access to a website where this could be posted...*

# Publication of negative results

- Bias automatically occurs if only positive results are reported!
- Negative results may be just as important for the scientific community, even if they are less newsworthy
- Many medical journals require registration of trials before they start, to prevent the under-reporting of negative results (<http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html>)

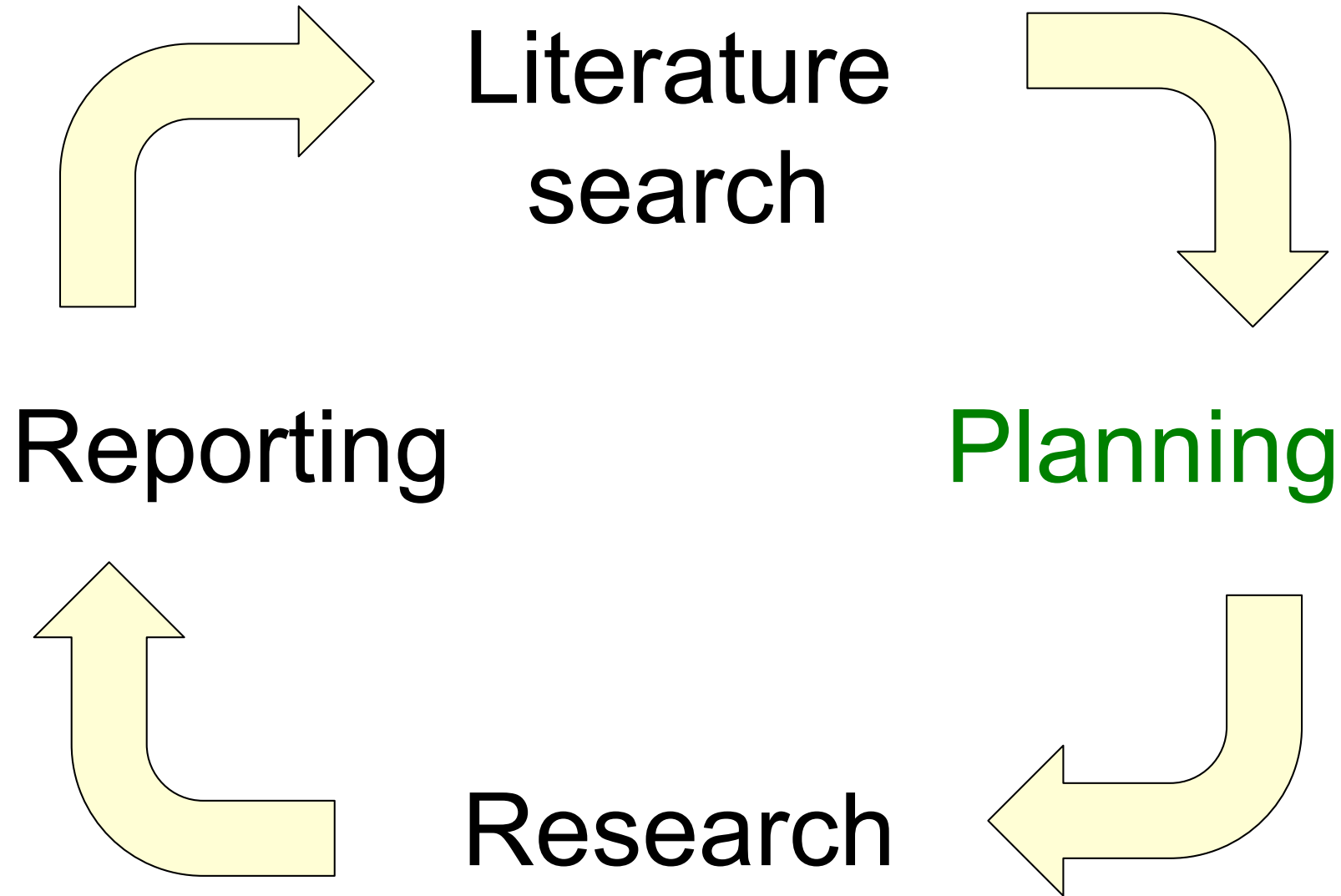
There are a number of journals now that report negative results, e.g.

J of Negative Results (<http://www.jnr-eeb.org/index.php/jnr>)

J of Negative Results in Biomedicine (<http://www.jnrbm.com>)

J of Pharmaceutical Negative Results (<http://www.pnrjournal.com>)

The All Results Journals (<http://www.arjournals.com/ojs>)



Identify and ensure the quality of (at least)  
the critical points in the experiment:  
critical for animal welfare and scientific value

# Good reporting and increased implementation of the 3Rs is dependent upon:

*Quality assurance and a culture of care at all levels of the animal facility.*

- SOPs describing good techniques, carried out by **competent** operators
- A Checklist (“contract”) between researcher and the facility
- The AAALAC **Program Description template** or something similar as an overall quality assurance checklist for the facility
- A **Master Plan** as a weekly checklist for the whole facility



# *Template for a Program Description from AAALAC International*

- Animal care and use policies and responsibilities
- Animal environment, housing and management
- Veterinary medical care
- Physical plant

<https://www.aaalac.org/programdesc/index.cfm>



---

AAALAC. Where science and responsible animal care connect.  
c. 2001 AAALAC International



[www.aaalac.org](http://www.aaalac.org)

## OUTLINE

### DESCRIPTION OF INSTITUTIONAL ANIMAL CARE AND USE PROGRAM

- I. Introduction
  - A. Name of Program Unit
  - B. Overview and Purpose
  - C. Description of the Organization (Attach organizational chart plus any support comments needed)
  - D. Key Institutional Representatives
  - E. Accreditation History
  - F. Nature of Research, Testing, and Teaching Programs
  - G. Research Funding Source(s)
  - H. Summary of Facilities
  - I. Other Units not Included in This Description
  - J. Contract Facilities
  - K. Other Relevant Background
- II. Description
  - A. Institutional Policies and Responsibilities
    - 1. Monitoring the Care and Use of Animals
      - a. Institutional Animal Care and Use Committee (s) (IACUC)
        - 1) Who appoints Committee/who is Institutional Official
        - 2) Composition/Frequency of Meetings/Responsibilities of the Committee





# Guidelines

e.g.

- ARRIVE, ILAR, ICLAS, LASA/APC
- GSPC
- Guidelines for specific types of animal research

reporting

Search

Enable synonyms and stemming

Reset

Database: 3R Guide Classic AVs NORINA TextBase

Search in: All Text Title Author Publisher Supplier Record Number

62 results

Order by: Relevance

**Guidelines for reporting the results of experiments on fish**  
**3R Guide/15075**  
A detailed account of experimental design, including an accurate description of the animals used, is an essential part of good research practice. This paper suggests guidelines for reporting fish experiments.

**Guidelines for reporting the results of experiments using mammals**  
**3R Guide/15076**  
A detailed account of experimental design, including an accurate description of the animals used, is an essential part of good research practice. This paper suggests guidelines for reporting experiments on mammals.

**Recommendations for the conduct, reporting, editing and publication of scholarly work in medical journals**  
**3R Guide/15093**  
The International Committee of Medical Journal Editors (ICMJE) developed these

**Category**

- ▢ Agricultural animals (8)
- ▢ Anaesthesia and analgesia (12)
- ▢ Aquatic animals (5)
- ▢ Behavioural research (6)
- ▢ Birds (7)
- ▢ Blood sampling (8)
- ▢ Cancer research (5)
- ▢ Design (31)
- ▢ Disease research (7)
- ▢ Education and training (10)
- ▢ Environmental enrichment (9)
- ▢ Ethics & harm-benefit analysis (17)
- ▢ Fish (8)
- ▢ Handling (14)
- ▢ Housing and management (27)
- ▢ Humane killing (15)
- ▢ Miscellaneous (1)
- ▢ Neuroscience research (2)
- ▢ Non-human primates (12)
- ▢ Nutritional research (1)
- ▢ Procedures (30)
- ▢ Reporting (19)
- ▢ Surgical research (10)
- ▢ Toxicology (6)
- ▢ Transport (8)
- ▢ Wildlife (8)

# The ARRIVE Guidelines

ITEM	RECOMMENDATION
Title	1 Provide as accurate and concise a description of the content of the article as possible.
Abstract	2 Provide an accurate summary of the background, research objectives, including details of the species or strain of animal used, key methods, principal findings and conclusions of the study.
<b>INTRODUCTION</b>	
Background	3 <ul style="list-style-type: none"> <li>a. Include sufficient scientific background (including relevant references to previous work) to understand the motivation and context for the study, and explain the experimental approach and rationale.</li> <li>b. Explain how and why the animal species and model being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.</li> </ul>
Objectives	4 Clearly describe the primary and any secondary objectives of the study, or specific hypotheses being tested.
<b>METHODS</b>	
Ethical statement	5 Indicate the nature of the ethical review permissions, relevant licences (e.g. Animal (Scientific Procedures) Act 1986), and national or institutional guidelines for the care and use of animals, that cover the research.
Study design	6 For each experiment, give brief details of the study design including: <ul style="list-style-type: none"> <li>a. The number of experimental and control groups.</li> <li>b. Any steps taken to minimise the effects of subjective bias when allocating animals to treatment (e.g. randomisation procedure) and when assessing results (e.g. if done, describe who was blinded and when).</li> <li>c. The experimental unit (e.g. a single animal, group or cage of animals).</li> </ul> A time-line diagram or flow chart can be useful to illustrate how complex study designs were carried out.
Experimental procedures	7 For each experiment and each experimental group, including controls, provide precise details of all procedures carried out. <p>For example:</p> <ul style="list-style-type: none"> <li>a. How (e.g. drug formulation and dose, site and route of administration, anaesthesia and analgesia used [including monitoring], surgical procedure, method of euthanasia). Provide details of any specialist equipment used, including supplier(s).</li> <li>b. When (e.g. time of day).</li> <li>c. Where (e.g. home cage, laboratory, water maze).</li> <li>d. Why (e.g. rationale for choice of specific anaesthetic, route of administration, drug dose used).</li> </ul>
Experimental animals	8 <ul style="list-style-type: none"> <li>a. Provide details of the animals used, including species, strain, sex, developmental stage (e.g. mean or median age plus age range) and weight (e.g. mean or median weight plus weight range).</li> <li>b. Provide further relevant information such as the source of animals, international strain nomenclature, genetic modification status (e.g. knock-out or transgenic), genotype, health/immune status, drug or test naïve, previous procedures, etc.</li> </ul>

Sample size	10 <ul style="list-style-type: none"> <li>a. Specify the total number of animals used in each experiment, and the number of animals in each experimental group.</li> <li>b. Explain how the number of animals was arrived at. Provide details of any sample size calculation used.</li> <li>c. Indicate the number of independent replications of each experiment, if relevant.</li> </ul>
Allocating animals to experimental groups	11 <ul style="list-style-type: none"> <li>a. Give full details of how animals were allocated to experimental groups, including randomisation or matching if done.</li> <li>b. Describe the order in which the animals in the different experimental groups were treated and assessed.</li> </ul>
Experimental outcomes	12 Clearly define the primary and secondary experimental outcomes assessed (e.g. cell death, molecular markers, behavioural changes).
Statistical methods	13 <ul style="list-style-type: none"> <li>a. Provide details of the statistical methods used for each analysis.</li> <li>b. Specify the unit of analysis for each dataset (e.g. single animal, group of animals, single neuron).</li> <li>c. Describe any methods used to assess whether the data met the assumptions of the statistical approach.</li> </ul>
<b>RESULTS</b>	
Baseline data	14 For each experimental group, report relevant characteristics and health status of animals (e.g. weight, microbiological status, and drug or test naïve) prior to treatment or testing (this information can often be tabulated).
Numbers analysed	15 <ul style="list-style-type: none"> <li>a. Report the number of animals in each group included in each analysis. Report absolute numbers (e.g. 10/20, not 50%).</li> <li>b. If any animals or data were not included in the analysis, explain why.</li> </ul>
Outcomes and estimation	16 Report the results for each analysis carried out, with a measure of precision (e.g. standard error or confidence interval).
Adverse events	17 <ul style="list-style-type: none"> <li>a. Give details of all important adverse events in each experimental group.</li> <li>b. Describe any modifications to the experimental protocols made to reduce adverse events.</li> </ul>
<b>DISCUSSION</b>	
Interpretation/ scientific implications	18 <ul style="list-style-type: none"> <li>a. Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature.</li> <li>b. Comment on the study limitations including any potential sources of bias, any limitations of the animal model, and the imprecision associated with the results<sup>2</sup>.</li> <li>c. Describe any implications of your experimental methods or findings for the replacement, refinement or reduction (the 3Rs) of the use of animals in research.</li> </ul>
Generalisability/ translation	19 Comment on whether, and how, the findings of this study are likely to translate to other species or systems, including any relevance to human biology.
Funding	20 List all funding sources (including grant number) and the role of the funder(s) in the study.



The ARRIVE Guidelines: Animal Research: Reporting of In Vivo Experiments. Originally published in PLOS Biology, June 2010<sup>1</sup>

<https://www.nc3rs.org.uk/arrive-guidelines>



# The ARRIVE guidelines

## Animal Research: Reporting of *In Vivo* Experiments

Carol Kilkenny<sup>1</sup>, William J Browne<sup>2</sup>, Innes C Cuthill<sup>3</sup>, Michael Emerson<sup>4</sup> and Douglas G Altman<sup>5</sup>

<sup>1</sup>The National Centre for the Replacement, Refinement and Reduction of Animals in Research, London, UK, <sup>2</sup>School of Veterinary Science, University of Bristol, Bristol, UK, <sup>3</sup>School of Biological Sciences, University of Bristol, Bristol, UK, <sup>4</sup>National Heart and Lung Institute, Imperial College London, UK, <sup>5</sup>Centre for Statistics in Medicine, University of Oxford, Oxford, UK

ARRIVE (动物研究: 体内实验报告) 指南是由国家3R中心创设,旨在通过提高动物研究设计,分析和报告的质量,使报告的信息量最大化并将不必要的研究减至最低程度。该指南于2010年6月在PLOS Biology 网络杂志发表,并得到多家科研杂志、主要的资助机构和学术团体的赞同。

### ARRIVE 指南的宗旨是:

- 提高动物研究报告的质量。
- 指导作者在稿件中提供必要的信息,但并不是硬性规定。
- 报告的灵活性使之广泛适应于各种研究领域和实验方案
- 促进具有可重复性、透明性、精确性、全面性、简明性、逻辑性的高质量论文。
- 促进科研成果在科学界更广泛的交流。

### ARRIVE 指南无意于:

- 促进统一性,扼杀创造性,或鼓励作者条条框框。有些条款并不适用于所有的研究,有些可用图表及说明或流程图展示(如所处理的,评估的和分析的动物数量)。
- 提供实验设计和执行的指南。但是指南中有些条款譬如随机化,施盲和使用对照组等对于设计实验时减少偏倚风险和提高研究的稳健性是有帮助的

### ARRIVE指南的适用对象是:

- 初涉写作或经验丰富的作者
- 杂志编辑
- 专业评审
- 资助机构

### ARRIVE指南适用于哪些科研领域?

- 最适用于比较研究,即两个或多个实验动物组进行比较,其中一组或多组常设为对照组。也适用于比较药物不同剂量的研究,或者如用单一动物作为其自身对照(被试内实验)。
- 大多数建议也适用于不舍对照组的任何领域。
- 适用于涉及实验动物生物科学研究的任何领域。

### 如何使用ARRIVE 指南?

该指南提供一个核对清单便于对准备发表的稿件进行准备和评审。

### 参考文献

1. Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG (2010) Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. PLOS Biol 8(6): e1000412. doi:10.1371/journal.pbio.1000412
2. Schulz KF, Altman DG, Moher D, the CONSORT Group (2010) CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMJ 340:c332.

### 资助

ARRIVE 报告指南项目是由国家3R (替代,优化,和减少使用动物进行研究) 中心 (NC3Rs) 资助

### 致谢

国家3R中心 (NC3Rs) 对所有在 ARRIVE 指南的创设中提供宝贵经验和建议的各位专家致以最衷心的感谢。特别感谢NC3Rs 报告指南工作组所有成员。我们同时要感谢NC3Rs 的基金持有者、医学研究委员会、生物技术和生物科学研究委员、威廉信托、帕金森氏病协会、英国心脏基金会,及其基金持有人和基金委员会成员对指南所提的反馈意见。

感谢胡晖编辑(《环境与健康展望》)、庞万勇博士(赛诺菲研发中心)和 吴东升博士(伦敦大学玛丽女王学院)帮助审核中文翻译。

### Further Information

[www.nc3rs.org.uk/ARRIVE](http://www.nc3rs.org.uk/ARRIVE)  
[enquiries@nc3rs.org.uk](mailto:enquiries@nc3rs.org.uk)  
@NC3Rs

***So we would find more 3R literature if there was greater transparency...***

Improved publication standards

Open Access to primary data and negative results

Clear implementation of the 3Rs

Editorial action

- More structured M&M sections in papers
- Information on the ethical review process and justification
- Experimental design and appropriate analysis
- Compliance with guidelines
  - ARRIVE, GSPC, ILAR, ICLAS, LASA/APC
  - local guidelines, AAALAC template
- <http://oslovet.norecopa.no/3R/produkter.aspx?search=reporting>
- Compliance with the Basel Declaration





[basel-declaration.org](http://basel-declaration.org)

- emphasises the 3Rs
- encourages transparency and collaboration to avoid repetition of animal studies
- implement and monitor the highest training standards
- invites animal welfare organisations to open discussion
- promotes balanced dialogue

***We would also find more 3R literature if there was greater use of 3R descriptors...***

Using PubMed to access data in MEDLINE:

MESH (Medical Subject Headings) thesaurus

The image displays three screenshots of PubMed search results, each with a red circle highlighting the search term and the total number of results. The first screenshot shows a search for "Animal Use Alternatives"[Mesh] resulting in 2989 results. The second screenshot shows a search for "Animal Testing Alternatives"[Mesh] resulting in 2635 results. The third screenshot shows a search for "Animal Experimentation"[Mesh] resulting in 6572 results. Each screenshot also shows the PubMed logo, RSS, Save search, and Advanced options, along with a summary and sorting menu.

Search Term	Number of Results
"Animal Use Alternatives"[Mesh]	2989
"Animal Testing Alternatives"[Mesh]	2635
"Animal Experimentation"[Mesh]	6572

Other databases have their own thesauri. A thesaurus can be useful to build up a list of suitable keywords, even if you use another database.

## ***Examples of 3R sources***

- ***National 3R centres***
- ***3R congress proceedings***
- ***Guidelines papers***
- ***Journals***
- ***Discussion groups***
- ***Training schools***

# National 3Rs Centres

The screenshot shows the homepage of the National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs). The top left features the NC3Rs logo and the full name of the organization. To the right, there are links for 'Login' and 'Register', along with social media icons for LinkedIn, Twitter, Facebook, and YouTube. A search bar is positioned below these links. The main navigation menu includes 'The 3Rs', 'Our science', '3Rs resources', 'Funding', 'News', 'Events', and 'About us'. The central content area is a carousel with three items: 1) A photograph of a laboratory with a teal overlay and the text 'An institutional framework for the 3Rs'. 2) A word cloud with 'nc3rs' and '3rs' as prominent terms, with a purple overlay and the text 'Our Science'. 3) A microscopic image of cells with a purple overlay and the text '2015 Funding Panel vacancies: now recruiting'. Navigation arrows are visible on the left and right sides of the carousel.

NC3Rs National Centre for the Replacement, Refinement & Reduction of Animals in Research

Login | Register

Search this site

The 3Rs | Our science | 3Rs resources | Funding | News | Events | About us

An institutional framework for the 3Rs

Our Science

2015 Funding Panel vacancies: now recruiting

[www.nc3rs.org.uk](http://www.nc3rs.org.uk)

# Canadian Council on Animal Care (CCAC)

+  
Guidelines for lab, farm, fish and wildlife research

HOME  
Send us your feedback  
Three Rs Microsite  
CCAC web site

Step-by-step Three Rs search strategy

**Quick Info**  
CCAC guidelines & policies on animal care protocols  
Where to do a Three Rs literature search  
Is your Three Rs Search complete?  
Animal use protocol worksheet

[www.ccac.ca](http://www.ccac.ca)

## Three Rs Search Guide

If you plan to use animals for scientific purposes, you must complete an animal use protocol and submit it to an animal care committee for approval prior to commencement of the study. The animal use protocol outlines how the Three Rs will be implemented in the proposed animal-based procedures. To find the most up-to-date information on the Three Rs, investigators typically conduct a structured information search. To assist investigators with this search, the CCAC has produced the Three Rs Search Guide.



The Three Rs Search Guide provides detailed instructions on how to conduct a Three Rs information search in the [Step-by-Step Three Rs Search Strategy](#).



# Animal welfare organisations

**RSPCA**  
ONLINE  
Campaigns  
Animal Care  
SEARCH  
ABOUT THE RSPCA  
ADVICE CENTRE  
NEWS  
CAMPAIGNS  
GOOD BUSINESS AWARDS  
ANIMAL CARE  
REHOMING  
HOW YOU CAN HELP  
EDUCATION  
SCIENCE GROUP  
FREEDOM FOOD  
LOCAL RSPCA  
RSPCA INTERNATIONAL  
PUBLICATIONS  
CAREERS  
UNDER 8TEENZ  
My RSPCA  
Help  
Local

AND ADVICE  
0300 1234

## Reducing suffering - Rabbit welfare

[back to research animals home](#)

**Thousands of rabbits are used in research and testing throughout the European Union every year, mostly in pharmaceutical research and development. The lives of laboratory rabbits can be greatly improved by providing housing and care that caters for their physical and behavioural needs.**

**UFAW/RSPCA Rabbit Behaviour and Welfare Group**

During 2008, the UFAW/RSPCA Rabbit Behaviour and Welfare Group published a report providing practical guidance on refining laboratory rabbit husbandry

### Reducing suffering: introduction

For as long as animals are used in research and testing, every step must be taken to reduce suffering and improve welfare... [more](#)

### Refinement

The research animals department promotes initiatives that will lead to improvements in laboratory animal housing and care and reductions in suffering caused by procedures... [more](#)

### Rodent welfare

Working to improve the welfare of laboratory rodents is extremely important because the vast majority of animals used in research and testing are mice and rats... [more](#)

### Rabbit welfare

The lives of laboratory rabbits can be greatly improved by providing housing and care that caters for their physical and behavioural needs... [more](#)

[www.rspca.org.uk/sciencegroup/researchanimals](http://www.rspca.org.uk/sciencegroup/researchanimals)



A resource book for  
lay members of ethical  
review and similar  
bodies worldwide

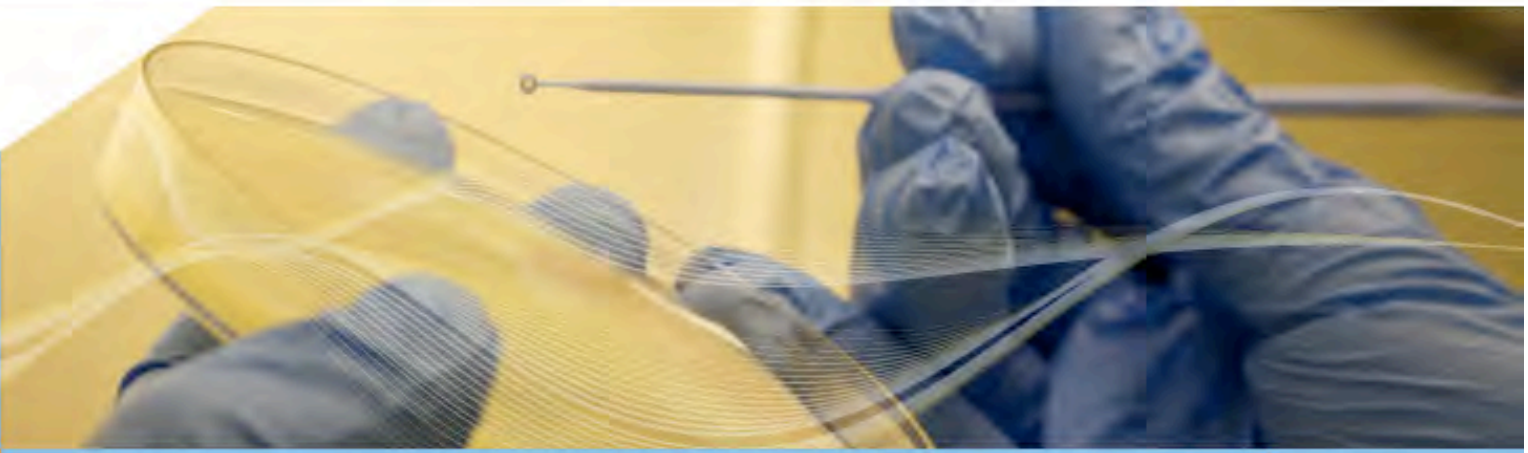
3rd edition  
January 2015

Maggy Jennings and Jane A. Smith





JOHNS HOPKINS  
BLOOMBERG  
SCHOOL OF PUBLIC HEALTH



the global clearinghouse for information on alternatives to animal testing

SEARCH ALTWEB

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RESOURCES ▶

ALTEX ▶

FEATURED ITEMS ▶

PUBLICATIONS ▶

NEWSLETTER ▶

ESPAÑOL ▶

CAAT HOME ▶



Chemical Information Day  
November 11, 2009

Network with scientific,  
industry, and regulatory experts  
from the US and Europe

**REGISTER NOW!**

## Search for Alternatives

A Detailed, Step-by-Step Guide to Alternatives Searches

### ALTERNATIVES NEWS

▶ [CAAT Chemical Information Day: Nov. 11, 2009: REGISTER NOW!](#)

Wed, 04 Nov 2009 16:31:06 GMT

▶ [ILAR to Publish Guidelines for Scientific Publications Involving Animal Studies](#)

Fri, 30 Oct 2009 20:18:49 GMT

▶ [October 2009 AltTox Digest Available](#)

Fri, 30 Oct 2009 16:35:01 GMT

### TOOLS

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### NEW ALTEX



[altweb.jhsph.edu](http://altweb.jhsph.edu)

# *Centres giving information on alternatives*



## UCCAA

University of California  
Center for Animal Alternatives



[www.lib.ucdavis.edu/dept/animalalternatives](http://www.lib.ucdavis.edu/dept/animalalternatives)



**Animal Welfare  
Information  
Center**

U.S. DEPARTMENT OF AGRICULTURE  
NATIONAL AGRICULTURAL LIBRARY

[awic.nal.usda.gov](http://awic.nal.usda.gov)

*Future collaboration: retrieval of specific, flagged 3R-records from a Unified Repository*



**Animal Welfare  
Information  
Center**

U.S. DEPARTMENT OF AGRICULTURE  
NATIONAL AGRICULTURAL LIBRARY

*accessing references from many of the large databases such as MEDLINE*

[norecopa.no](http://norecopa.no)    [awic.nal.usda.gov](http://awic.nal.usda.gov)

*The world congresses on the 3Rs are important 3R-drivers and disseminators of information:*

[wc9prague.org](http://wc9prague.org)

*891 abstracts, 49 countries, 1000 participants  
(the next one is in September 2017 in Seattle)*

*1996: 2nd World Congress on Alternatives and Animal Use in the Life Sciences, Utrecht*



*1997: Altweb (Alternatives to animals on the web)*

<http://altweb.jhsph.edu>



## ***International consensus meetings***

*Harmonisation of the Care and Use of:*

*Fish (2005)*

*Wildlife (2008)*

*Fish (2009)*

*Agricultural animals (2012)*

[\*http://norecopa.no/consensus-meetings\*](http://norecopa.no/consensus-meetings)

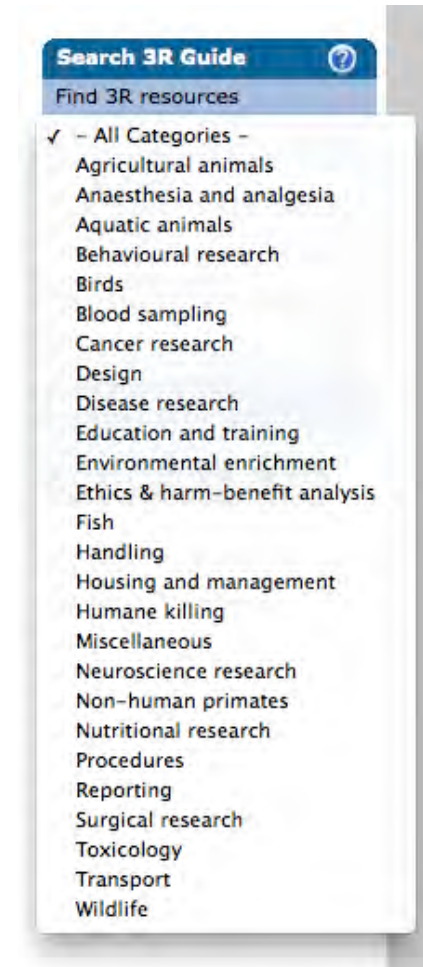
*All presentations and consensus statements are on  
the internet: a lasting resource*

# ***Guidelines as a portal to more information***

*R Johansen, JR Needham, DJ Colquhoun, TT  
Poppe & AJ Smith*

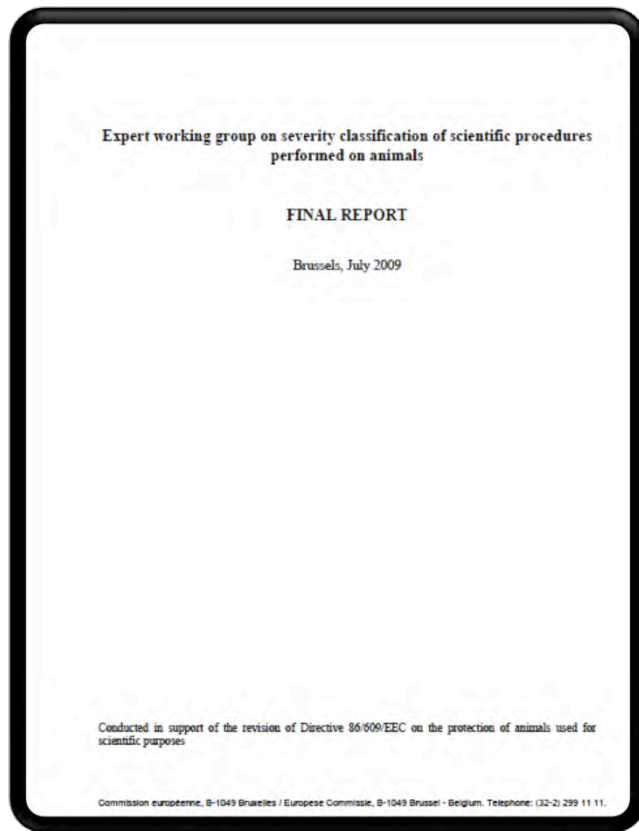
## ***Guidelines for health and welfare monitoring of fish used in research***

Laboratory Animals, 2006, 40: 323-340  
<http://www.lal.org.uk/pdffiles/GuidelinesFish.pdf>



**For a global view of guidelines, see 3R Guide:**

[http://oslovet.norecopa.no/3R/produkter.aspx?type=66\\_Guidelines](http://oslovet.norecopa.no/3R/produkter.aspx?type=66_Guidelines)



## ***Expert Working Group report on severity classification***

[http://ec.europa.eu/environment/chemicals/lab\\_animals/pdf/report\\_ewg.pdf](http://ec.europa.eu/environment/chemicals/lab_animals/pdf/report_ewg.pdf)



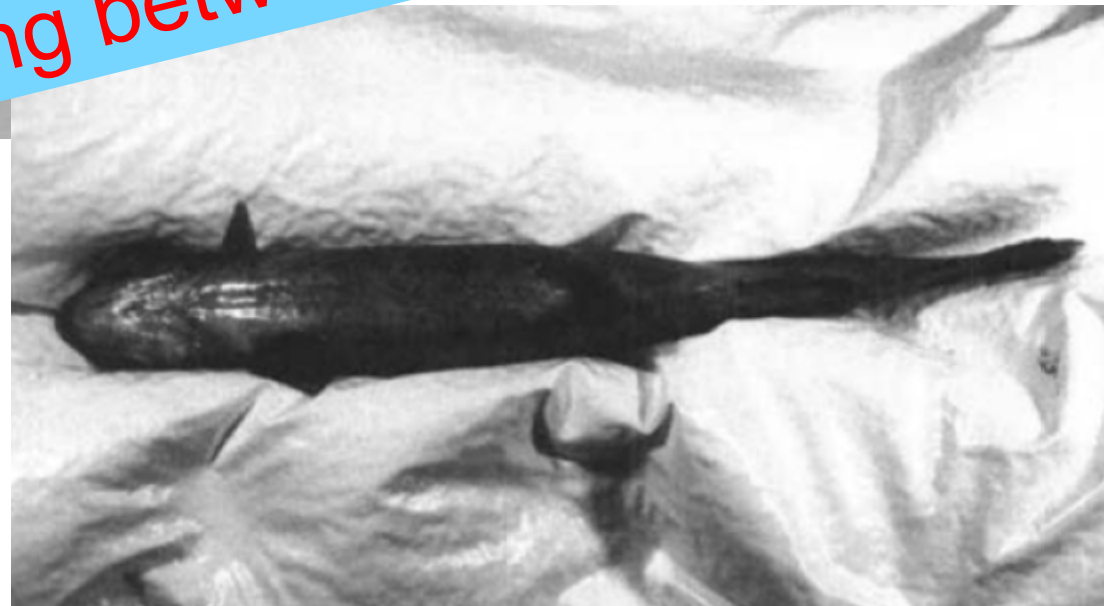
# Methods of positioning fish for surgery or other procedures out of water

**Trond Brattelid & Adrian J. Smith**

Laboratory Animal Unit, Norwegian School of Veterinary Science, PO Box 8146 Dep., N-0033 Oslo, Norway



**Lateral thinking between species**



Laboratory Animals, 2000, 34,  
430-433

# We need more guidelines for specific research areas



## Guidance on the severity classification of procedures involving fish

P Hawkins, N Dennison, G Goodman, S Hetherington, S Llywelyn-Jones, K Ryde and AJ Smith

Laboratory Animals, 45: 219-224, 2011  
[www.norecopa.no/categories](http://www.norecopa.no/categories)

# Position Statements and Guidelines

- Food deprivation
- Toe clipping
- Pain relief
- Fin clipping of fish
- Biometric methods of identification
- Methods for identification of birds



The screenshot shows the Norecopa website, which is a Norwegian consensus platform for replacement, reduction, and refinement of animal experiments. The page is titled "Position statements" and is part of the "3Rs resources" section. The main content area lists several position statements: "Toe clipping in mice", "Pain relief in rodents", "Food deprivation in rodents", and "Student essays". Each statement includes a brief description of the topic and a link to the full document. The website also features a sidebar with navigation links, a search bar, and a footer with contact information.

**norecopa**  
Norwegian consensus platform for replacement, reduction and refinement of animal experiments

» > 3Rs resources > Position statements

## Position statements

Norecopa produces position statements on topics related to the use of animals in research and the 3Rs.

**Toe clipping in mice**  
The Norwegian Animal Research Authority asked Norecopa to evaluate toe clipping as a means of identification and tissue sampling in mice. The Board produced an 18-page document, which has been circulated to all members. [A translation of the final version can be downloaded here.](#) The document includes an evaluation of alternative methods for the identification and genotyping of rodents, with a literature references. The Board composed a [supplementary statement](#) in March 2010 following three new published studies, which was circulated to its members.

**Pain relief in rodents**  
In collaboration with colleagues in the laboratory animal environment, Norecopa has produced a document on [pain relief in rodents](#).

**Food deprivation in rodents**  
Norecopa has written an 11-page position statement on food deprivation in rodents. [The summary \(recommendations\) can be read here.](#) [The full document is available here.](#)

**Student essays**  
Norecopa has edited essays on [Fin clipping in fish](#), [Biometric methods of identification](#) and [Guides to identification methods for birds](#), in connection with a course in laboratory animal science for researchers. These essays have not been quality-controlled, nor is the content necessarily endorsed by Norecopa. Updated versions of the essays will be published here, if we receive feedback from readers. The contents of these essays may be used freely, but it must not be presented as representing the views of Norecopa or its secretary. Furthermore, the factual content (including literature references) should be checked before use.

Would you like Norecopa to write a statement about a topic related to your research?  
[Please contact the secretary!](#)

Norecopa also produces political statements and writes newspaper articles about animal research and the 3Rs. [These can be read here.](#)

**Hvem er vi?**  
Om Norecopa  
Historikk  
Informasjonsmaterieill  
Ofte stilte spørsmål  
Styre og sekretariat  
Vedtekter  
Styrets intranett

**Hva gjør vi?**  
Aktivitetsplan  
Årsmøter  
Faglige uttalelser  
Konsensusmater  
Norecopas 3R-pris  
Regnskap  
Styrereferater

**Bli medlem!**  
Medlemmer  
Medlemsfordeler  
Nyhetsbrev  
Tegn medlemskap!

**English section**  
About Norecopa  
Activities

**3Rs resources**  
Categories of severity  
Consensus meetings  
Guidelines A-Z  
Position statements  
Statistical design  
Textbase: literature on lab animal science  
The Concept of the 3Rs  
The NORINA database of audiovisual alternatives in teaching and training

**Dyr i forskning**  
Å planlegge dyreforsøk  
Fisk  
Husdyr  
Laboratoriedyr  
Vilt

**Om Norecopa**  
Norecopa arbeider for å fremme "de 3 R'ene" i forskningen som kan involvere dyr:  
**\* Replace**  
**\* Reduce**  
**\* Refine**  
Norecopa tilstreber konsensus om de tre R'ene mellom alle de fire interessepartene rundt dyreforskning:

Forvaltningen  
Industrien  
Forskningen  
Dyreforskning

**Norecopa**  
Norwegian Veterinary Institute  
P.O.Box 750 Sentrum  
N-0106 Oslo, Norway

**Visiting address:**  
Ullevålsveien 68  
0454 Oslo  
Org.no. 992 199 199

Tel: +47 41 22 09 49  
Fax: +47 23 21 60 01  
post@norecopa.no  
www.norecopa.no

Utviklet av Netlab  
Oppdateres med  
redaktør



# Position Statements from the Norwegian Animal Research Authority



## FORSØKSDYRUTVALGET



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[Arkiv](#)

[Om forsøksdyrutvalget](#)

[Regelverk](#)

[Prinsippavgjørelser ▶](#)

[For søkere](#)

[Kurs og kompetansekrav](#)

[Ofte stilte spørsmål](#)

[Alternativ til forsøk med dyr](#)

[Lenker](#)

[Møtevirksomhet](#)

[Kontakt oss](#)

- [03.07.14] [Prinsipputtalelse om bruk av telemetri](#)
- [03.07.14] [Prinsipputtalelse om bruk av telemetri-halsbånd på hjortevilt og rovvilt](#)
- [25.10.13] [Søknadspåttalelse ved blodprøvetaking av viltlevende fugler](#)
- [03.09.13] [Prinsipputtalelse: Merking av viltlevende fugler](#)
- [29.11.12] [Prinsipputtalelse om blokkersøknader](#)
- [23.10.12] [Merkeprosedyrer på fisk i laboratorieforsøk](#)
- [28.09.11] [Krav til avdelinger som ønsker å bli godkjente forsøksdyrvirksomheter](#)
- [18.03.11] [Retningslinjer for behandling av søknader om forsøk med lakselus](#)
- [23.02.11] [Belastende forsøk med smågnagere](#)
- [27.10.10] [Alle søknader som involverer lakselus skal inntil videre behandles av FDU](#)
- [03.04.09] [Smitteforsøk og smertevoldende forsøk på fisk](#)
- [21.01.08] [Bruk av Nevromusklære blokkere til Forsøksdyr](#)
- [14.11.08] [Forsøksdyr med ein avvikende fenotype \(genmodifiserte dyr, mutanter og innavlta linjer\)](#)
- [24.05.06] [Utviklingsstadium for fiskelarver som omfattes av regelverk for forsøksdyr.](#)
- [02.06.04] [Avlaving av gnagere med CO2](#)
- [02.06.04] [Giftighetstesting på fisk i petroleumsvirksomheten](#)
- [26.08.03] [Utfasing av LD50 - akutt giftighets testing](#)
- [21.07.03] [Forsøk med dyr for å illustrere kjent kunnskap \(inkl. undervisning\)](#)
- [21.07.03] [Oppstalling av smågnagere i metabolismebur](#)
- [21.07.03] [Veiledning for beredskapsvakt utenom ordinær arbeidstid ved Forsøksdyravdelinger](#)
- [11.12.02] [Bruk av eter til bedøvelse](#)
- [11.12.02] [Forsøksdyrutvalgets policy ved smertevoldende dyreforsøk](#)
- [03.07.02] [Bruk av intraperitoneale radiosendere](#)
- [10.05.02] [Produksjon av monoklonale antistoffer \(MAbs\)](#)
- [10.05.02] [Avlivningsprosedyrer for nyfødte smågnagere](#)

<http://www.mattilsynet.no/fdu/prinsippavgjorelser>

European Commission

ENVIRONMENT

European Commission > Environment > Chemicals > Animals used for scientific purposes

Home About us Policies Funding Legal compliance News & outreach

**Animals used for scientific purposes**

**Retrieval and provision of information on the "Three Rs" and alternatives**

Accessing accurate, relevant and up-to-date information on the Three Rs is a challenge for all those use of animals.

**Legislation and implementation**

- EU legislative framework
- Implementation of Directive 2010/63/EU
- Q&A and guidance documents

**The "Three Rs" and alternative approaches**

- Replacement, Reduction and Refinement – the "Three Rs"
- Validation, acceptance and use
- EU activities to advance alternatives
- Member State activities to advance alternatives
- Finding and distributing information on alternatives
- Key resources
  - Search Tools
  - Databases
  - Portals and web-sites
  - Journals
  - Other resources and organisations

**Animals used for scientific purposes**

**Opinions of European Commission Expert Committees related to the use of animals in experiments**

Facebook Twitter

## ***European Directive, Article 47: 3R-alternative approaches***

- 1. The Commission and Member States shall **contribute** to the development and validation of 3R-alternatives, and encourage research in this field*
- 2. Member States shall **assist** the Commission in identifying laboratories for validation studies*
- 3. The Commission shall set the priorities for these studies and **allocate** tasks*
- 4. Member States shall **promote** alternatives and **disseminate** information on them*
- 5. Member States shall nominate a single point of contact to provide **advice** on the regulatory relevance and suitability of alternatives proposed for validation (PARERE: **P**reliminary **A**ssessment of **R**egulatory **R**elevance)*

# ***Journals***

*ATLA (Alternatives to Laboratory Animals)*

*Animal Welfare (UFAW)*

*ILAR Journal*


*Laboratory Animals*

*Comparative Medicine*

See [www.3RGuide.info](http://www.3RGuide.info) for more



It doesn't have to be the latest issue or most recent report...

THE NATIONAL ACADEMIES  [Current Projects](#) [Publications](#) [Directories](#) [Search](#) [Site Map](#) [Feedback](#)

[ILAR HOME](#)  
[ILAR JOURNAL ONLINE](#)  
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[Volume 43 - 2002](#)  
[Volume 42 - 2001](#)  
[Volume 41 - 2000](#)  
[Volume 40 - 1999](#)  
[Volume 39 - 1998](#)  
[Volume 38 - 1997](#)  
[Volume 37 - 1995](#)  
[ILAR News -- Volume 36 and previous](#)

**ILAR Journal Volume 41(2)**

- [Contents](#)
- [Front Matter](#)

**ILAR** NATIONAL RESEARCH COUNCIL  
INSTITUTE FOR LABORATORY ANIMAL RESEARCH

**Journal**

**Volume 41, Number 2 2000**

A publication for biomedical investigators, laboratory animal scientists, institutional officials for research, and members of animal care and use committees.

**Humane Endpoints for Animals Used in Biomedical Research and Testing**

[Translation Guidelines for ILAR Reports](#)  
[ILAR's Home Page](#)  
[Introduction: Reducing Unnecessary Pain and Distress in Laboratory Animals Using Humane Endpoints](#)  
*William S. Stokes*  
[Recognizing Pain and Distress in Laboratory Animals](#)  
*E. Carstens and Gary P. Moberg*  
[Defining the Moribund Condition as an Experimental Endpoint for Animal Research](#)  
*Linda A. Toth*  
[A Systematic Approach for Establishing Humane Endpoints](#)  
*David B. Morton*  
[Humane Endpoints and Cancer Research](#)  
*James Wallace*  
[Humane Endpoints for Genetically Engineered Animal Models](#)  
*Melvin B. Dennis, Jr.*  
[Humane Endpoints for Infectious Disease Animal Models](#)  
*Ernest D. Ofert and Dale L. Godson*  
[Refinement of Vaccine Potency Testing with the Use of Humane Endpoints](#)  
*Coenraad F.M. Hendriksen and Björn Steen*  
[Humane Endpoints and Acute Toxicity Testing](#)

<http://ilarjournal.oxfordjournals.org>

# *Email discussion groups*

*e.g. CompMed + archive  
LAREF  
VOLE  
Local competent persons...*

See [www.3RGuide.info](http://www.3RGuide.info) for more

## FRAME Training Schools

Portugal, 30 March-1 April 2015  
Norway, February 2016

[www.frame.org.uk/training-schools](http://www.frame.org.uk/training-schools)



NC3Rs website

<http://nc3rs.org.uk/experimental-design>



# Guidelines for the Design and Statistical Analysis of Experiments Using Laboratory Animals

<http://ilarjournal.oxfordjournals.org/content/43/4/244.full>

## NC3Rs Experimental Design Assistant (EDA)

<http://nc3rs.org.uk/experimental-design-assistant-eda>



<http://www.uk.sagepub.com/books/Book242188?siteId=sage-uk&prodTypes=any&q=9781853155130>

## TextBase

### TextBase publications

Your search for TextBase publications containing the text "design" in the title returned the following results (13 items, page 1 of 1):

**The Design of Animal Experiments: Reducing the Use of Animals in Research Through Better Experimental Design.** By Festing, Michael F.W.; Overend, Philip, Das, Rose Gaines; Borja, Mario Cortina & Berdoy, Manuel (2002). This handbook is aimed at all research scientists who use laboratory animals, with the aim of helping them to design their own experiments more effectively and/or to improve their ability to communicate with professional statisticians when designing more complex experiments.

**CCAC Guidelines on: Laboratory Animal Facilities - Characteristics, Design, and Development.** By Neil, David and McKay, Donald, with the collaboration of the CCAC Facilities Standards Subcommittees (2003). This document concentrates on the characteristics of a laboratory animal facility and hence do not cover all subjects matter discussed in the "Guide to the Care and Use of Experimental Animals", Volume 1, Chapters II and III, (CCAC, 1993).

**Experimental Design and Analysis in Animal Sciences.** By Morris, Tim R. (1999). This guide includes information for the design and analysis of experiment in animal science.

**Experimental Design: A Handbook and Dictionary for Medical and Behavioral Research.** By Krauth, J. (2000). Scientists planning experiments in medical and behavioural research will find this handbook and dictionary an invaluable desk reference tool.

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