Alternatives to the Use of Animals, and the Three Rs

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www.norecopa.no

Norecopa

National Consensus Platform for the Replacement, Reduction and Refinement of Animal Experiments



a competence centre for the 3RS

- What is an alternative, and what types do we have?
- Where and how do we find information about them?
- Why is it hard to find and what can we do about?
- Examples of 3R sources
- Tools for searching the literature



Reporting

Planning



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



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Missing mice: gaps in data plague animal research

Reports of hundreds of biomedical experiments lack essential information.

Monya Baker

05 January 2016

NATURE | NEWS

Rights & Permissions

Two studies have unveiled widespread flaws in the reporting of animal experiments — the latest in a series of papers to criticize shoddy biomedical research.

Whereas reports of clinical trials in major medical journals routinely state how many patients die or drop out of analysis during the course of a study, animal studies generally fail to report this figure — or drop animals without saying why, according to a team led by Ulrich Dirnagl at the Charité Medical University in Berlin. That lapse could significantly bias results, the team reports in the journal *PLoS* Biology¹.

In a second study in the same journal², a team led by John Ioannidis, an epidemiologist at Stanford University in California who has repeatedly called for more reproducible and transparent research, criticizes the lack of data availability and detailed protocols in biomedical papers.

What is an alternative?

A method without the use of animals that gives the same answers as an animal experiment.

Are these alternatives?

- Cell cultures
- Use of bacteria to test carcinogenicity
- Chemical analysis of biologically active compounds

N.B. Animal experiments are usually needed to develop and validate alternatives.

The potential for using alternatives

- Basic research: + / -
- Toxicological research ++
- Education & training +++ (very dependent upon objectives)
- Production and testing ++++

EU Directive Article 4: Principle of replacement, reduction and refinement

Member States shall ensure

- 1. that, wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure
- 1. that the number of animals used in projects is reduced to a minimum without compromising the objectives of the project
- 1. refinement of breeding, accommodation and care, and of methods used in procedures, eliminating or reducing to the minimum any possible pain, suffering, distress or lasting harm to the animals.

Article 13: Choice of methods

- National legislation can prohibit certain types of methods, and Member States shall ensure that a procedure is not carried out if a method not involving live animals is recognised by the EU
- 1. When choosing between procedures, select those which to the greatest extent
 - a) use the **minimum number**
 - b) use animals with the **lowest capacity** to experience pain, suffering, distress or lasting harm
 - c) cause the least pain, suffering, distress or lasting harm and are most likely to provide satisfactory results
- 2. Replace death as an end-point as far as possible with early and humane endpoints so as to:
 - a) result in the deaths of as few animals as possible
 - b) reduce the duration and intensity of suffering to the minimum possible and as far as possible ensure a painless death

Article 16: Reuse

An animal may only be reused if

- The actual severity of the previous procedures was mild or moderate
- The animal's general state of health and well-being has been restored
- 1. The next procedure is classified as mild, moderate or nonrecovery
- 1. It is in accordance with veterinary advice, taking into account the **lifetime experience** of the animal

In exceptional cases (after a veterinary examination) the competent authority can make an exception from point 1 and allow reuse if an animal has not been used more than once in a procedure entailing **severe** pain, distress or equivalent suffering

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
- 1. Member States shall assist the Commission in identifying laboratories for validation studies
- 1. The Commission shall set the priorities for these studies and allocate tasks
- 1. Member States shall promote alternatives and disseminate information on them
- Member States shall nominate a single point of contact to provide advice on the regulatory relevance and suitability of alternatives proposed for validation (PARERE: Preliminary Assessment of Regulatory Relevance)

ec.europa.eu/animals-in-science



1) Replacement alternatives

Computer simulations Films, video, virtual reality Models, 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, including plants Acute experiments (terminal anaesthesia) Trials on dead animals (ethically sourced cadavers, slaughterhouse material) Observation of animals in their natural setting or a brief period of captivity Animals in need of clinical veterinary care Research animals that will be used anyway Surplus breeders from lab animal suppliers Trials on humans (microdosing and medical imaging) Synthesis of new evidence from experiments that have already been performed Replacement with a theoretical session

Choose your objectives!

You can't decide whether or not there is an alternative until you know the aim of the experiment.

- 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)
- group work
- 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/s2memberfiles/32_S1a_3_Plenary_specialcontribution.pdf (pages 16-26, free registration required)







Simulator for training in sterilisation of the bitch (Rescue Critters)



Simulator for keyhole surgery https://www.3-dmed.com **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







'We may need the animals, as it were, on the night; but the machines will do very well at rehearsals'

"Alternatives" may be too poor to replace animals totally, but may be excellent as briefing or debriefing aids.

https://norecopa.no/education-training/films-and-slide-shows

Immobilisation and i.p. injection



Replacement alternatives in science

A paradigm shift is underway



Lung-on-a-chip Wyss Institute, Harvard



Next generation Multi-Organ-Chip



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



Organoids

e.g. Mini-livers



http://www.nc3rs.org.uk/news/mini-livers-showpromise-reduce-animal-use-science

Dr Meritxell Huch, Cambridge University

Adult mouse stem cells expand into fully functioning 3D liver tissue.

Cells from one mouse could be used to test 1000 drug compounds to treat liver disease, and reduce animal use by up to 50,000.

When implanted into mice with liver disease they continued to grow, extending the survival of the mice.

Next stage is human cells: liver research and transplantation





1997



https://en.wikipedia.org/wiki/Vacanti_mouse

http://www.nature.com/nbt/journal/vaop/ncurrent /full/nbt.3413.html

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





High Throughput Screening (HTS)



Cell culturing and compound management laboratories



Robotic platform with high-throughput liquid handler for sample preparation, dilution and test-plate treatment. Supported by optical plate reader, plate washer and incubator



Supported by optical plate reader, plat washer and incubator Data management system to trace

Automated imaging microscope can be added for high-content screening

Data management system to trace and process the test data

https://eurl-ecvam.jrc.ec.europa.eu/laboratories-research/high-throughput-screening-and-test-development/hts

Some of the reasons why industry still uses animals:

- 1. Regulatory requirements
- 2. Lack of validated alternatives
- 3. Risk of litigation

Some of the reasons why industry prefers alternatives:

- 1. In vitro methods are cheaper
- 2. They are faster
- 3. They are more reproducible

The problem:

- Despite rigorous testing, failures still occur
- Many of these occur at a late stage sometimes after the drug is on the market
- Many of these late failures lead to serious human disease or death
- Compounds fail in people with several diseases, which are impossible to model in an animal test system





colourbox.com

Learning new information without animal experiments by Synthesis of Evidence:

Systematic Reviews of ones that have already been published!

2) Reduction alternatives

A good statistician is the laboratory animal's best friend. Combined with efforts to reduce experimental "noise".



http://norecopa.no/norecopa/vedlegg/Berdoy-handout.pdf

Sources of experimental "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

FRAME Training Schools

Voss, 1 – 3 February 2016

www.frame.org.uk/training-schools



NC3Rs website

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



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



https://uk.sagepub.com/en-gb/eur/design-of-animalexperiments/book242188

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.



oslovet.norecopa.no/textbase
3) Refinement alternatives

"Simple" techniques?



Photo: NMBU

Are they feasible? For example, intramuscular injections

"Simple" identification methods? Do they affect the animal?



Photo: T. Poppe, NMBU



http://blogs.discovermagazine.com/notrocketscience/2011/01/12/fl ipper-bands-impair-penguin-survival-and-breedingsuccess/#.VLU6_8Y7_wo



Photo: colourbox.com

Norecopa's Annual Meeting Oslo, 24 May 2016:

Professor Rory Wilson, Swansea:

Putting tags and transmitters on birds:

are our guidelines flights of fancy?

https://norecopa.no/about-norecopa/annual-meetings

Refinement to avoid **contingent suffering**

(not just direct suffering caused by the procedure)

e.g. fear, boredom, discomfort

which may caused by

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



The Lonely Mouse

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

Increased hypothermia in response to treatment with a serotinergic agonist

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0 111065

http://www.labtimes.org/editorial/e_575.lasso

Evaluation of EMLA Cream for Preventing Pain during Tattooing of Rabbits: Changes in Physiological, Behavioural and Facial Expression Responses

Stephanie C. J. Keating, Aurelie A. Thomas, Paul A. Flecknell, Matthew C. Leach 🖾

PLoS ONE, 2012, 7(9): e44437. doi:10.1371/journal.pone.0044437

In a crossover study, eight New Zealand White rabbits each underwent four different treatments of actual or sham ear tattooing, with and without prior application of a topical local anaesthetic (lidocaine/prilocaine). Changes in immediate behaviour, heart rate, arterial blood pressure, serum corticosterone concentrations, facial expression and home pen behaviours were assessed. Changes in facial expression were examined to develop the Rabbit Grimace Scale in order to assess acute pain. Tattooing without EMLA cream resulted in significantly greater struggling behaviour and vocalisation, greater facial expression scores of pain, higher peak heart rate, as well as higher systolic and mean arterial blood pressure compared to all other treatments. Physiological and behavioural changes following tattooing with EMLA cream. Behavioural changes 1 hour post-treatment were minimal with no pain behaviours identifiable in any group. Serum corticosterone responses did not differ between sham and tattoo treatments.

Conclusions

Ear tattooing causes transient and potentially severe pain in rabbits, which is almost completely prevented by prior application of local anaesthetic cream. The Rabbit Grimace Scale developed appears to be a reliable and accurate way to assess acute pain in rabbits.

Grimace Scales



Facial Coding Unit Score Orbital Tighten 0 Cheek Flattening 0 Pointed Nose Whisker Change Total Pain Score:

a.



Facial Coding Unit	Score
Orbital Tightening	2
Cheek Flattening	1
Pointed Nose	2
Whisker Change	2

Total Pain Score:

b.

Think "3R-Alternatives" at all stages

- Breeding
- Transport
- Acclimation
- Procedures, e.g. choice of
 - dose
 - method of administration
 - methods of data collection (blood sampling, body temperature, heart rate, blood pressure etc.)
- Pilot studies

Consult the technicians from Day 1:

- they know the possibilities (and limitations) in the animal facility
- they often possess a large range of practical skills and are good at lateral thinking
- they know the animals best
- the animals know them best



The 3	Rs
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Our science

Funding

3Rs resources

Home > News > Blog > Creating a culture of care

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



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.

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



Training for new staff

Quality assurance and a culture of care at all levels of the animal facility will increase implementation of the 3Rs

- SOPs describing good techniques, carried out by competent operators
- Checklist ("contract") between researcher and the facility
- The AAALAC Program Description template* as an overall performance checklist
 - Institutional policies on animal care and use
 - Animal environment, housing and management
 - Veterinary care
 - Physical plant
- A Master Plan as a weekly checklist for the whole facility during the year

+ the necessary literature/resources/finances/support to implement these

*https://www.aaalac.org/programdesc/index.cfm



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.

Smith AJ & Hawkins P: Good Science, Good Sense and Good Sensibilities: The Three Ss of Carol Newton Submitted to *Animals*, August 2016.

Norecopa's website is designed to aid scientists in finding global 3R resources



advance the 3Rs

Searching for alternatives

- What's the problem? We have Google!
- How you can improve the situation
- Principles of setting up a search
- Resources to help you

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 3Rdatabases
- Scientists rarely use "3R" words when they write titles/abstracts/keywords for their papers
- Databases rarely flag 3R-papers with explicit thesaurus terms ^(B)
- We have no single "Journal of Alternatives"

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.

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.



Does the Internet give us everything we need to know on alternatives?



The Surface Web

The Deep (Invisible) Web

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What is the Surface Web useful for?

- Searching for a specific document which we know exists
- Looking for a starting-point for information on a specific topic
- Finding "grey literature" (e.g. unpublished reports)

The Deep Web

Many times larger than the Surface Web, material may be:

- Encrypted
- Registration/subscription
- Password or Captcha protected databases
- Dynamic, contextual or scripted webpages
- Unlinked content
- Not formatted for, or accessible by, standard search engines e.g. text in image or video files
- Material on company intranets



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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



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.

Principles of setting up a search

- Efficiency minimise the number of irrelevant or poor-quality results
- Effectivity maximise the number of high-quality results

Systematic Reviews

 The process of systematically locating, evaluating and synthesizing evidence from scientific studies in order to obtain a reliable overview

Synthesis of evidence by **meta-analysis**

The use of statistical methods to summarize the results of independent studies

Guidelines for systematic reviews:

http://3rs.ccac.ca/en/research/systematic-reviews.html

A step-by-step guide to systematically identify all relevant animal studies:

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3265183



Read! A step-by-step guide to systematically identify all relevant animal studies http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3265183 Construct and try out search strategies for each of the four **Search Components** (SC):

- 1. Intervention/exposure
- 2. Outcome measures
- 3. Animal population to be studied
- 4. Health problem of interest

e.g.

The effect of (SC1) group-housing on (SC2) blood pressure in (SC3) rats used in (SC4) diabetes research

Only then combine into one search string: SC1 AND SC2 AND SC3 (AND SC4)



Identifying search terms: Thesauri and synonyms

A thesaurus is a closed list of terms used to index and search databases. Often a good idea to start a search with a database using a thesaurus.

- "animal use alternatives" in the NLM MeSH (Medical Subject Headings) used by MEDLINE/PubMed
- NAL's thesaurus for alternatives to animals http://www.nal.usda.gov/awic/alternatives/alternativeanimalusethesaurus.htm
- EURL ECVAM's thesaurus (focus on *in vitro* toxicology): http://ecvam-dbalm.jrc.ec.europa.eu/f_main.cfm?idmm=7

Alice Tillema, Radboud University: How to construct a literature search

http://norecopa.no/how-to-construct-a-literature-search.pdf

How to construct a literature search Alice Tillema, Medical Library, Nijmegen

http://libguides.ru.nl/norecopa



Radboudumc

Radboud Universiteit 💮

Universiteitsbibliotheek

Radboud University / LibGuides / Norecopa - Literature Search / Search tips

Norecopa - Literature Search: Search tips

Start page for Norecopa AGM 24 May 2016

Search tips Home Search Guide PubMed SYRCLE ECVAM Search Guide (see A step by step guide PubMed Practical Download Content) to systematically find all relevant PubMed with incorporated animal filter (SYRCLE) animal studies How to construct a comprehensive search strategy SYRCLE Tools and support for systematic reviews THE FLIRL ECVAN SEARCH GLIDE · Formulate a specific research question DATA RETRIEVAL PROCEDURES SYRCLE Training materials for **Basic Principles** In animal models for Alzheimer's Disease what is the effect of Re Little supplementation of omega-3 fatty acids on cognition and Systematic Review workshop neurodegeneration? Determine which elements of the question will be your search components (SC) animals, alzheimer, omega 3 fatty acids Make a list of search terms** for every SC containing MeSH term e.g. alzheimer disease[MeSH] synonyms e.g. alzheimer, alzheimer's, alzheimers, dementia NAMES IN Create a search string for each SC using OR between the search terms Search string for component Alzheimer at SYRCLE website. Perform searches with separate search strings in PubMed Use History (Advanced) to combine search strings with AND. Example

• 🔀 ** Tips for turning a list of search terms into a search string (in Word)

LibGuides

Find other LibGuides Search

A step-by-step guide to systematically identify all relevant animal studies

Marlies Leenaars¹, Carlijn R Hooijmans¹, Nieky van Veggel^{1,2}, Gerben ter Riet³, Mariska Leeflang⁴, Lotty Hooft⁵, Gert Jan van der Wilt⁶, Alice Tillema⁷ and Merel Ritskes-Hoitinga¹



Figure 1 Combining components in the search strategy (adapted from Higgins and Green³)

Text search filter:

("animal experimentation" [MeSH Terms] OR "models, animal" [MeSH Terms] OR "invertebrates" [MeSH Terms] OR "Animals" [Mesh:noexp] OR "animal population groups" [MeSH Terms] OR "chordata" [MeSH Terms:noexp] OR "chordata, nonvertebrate" [MeSH Terms] OR "vertebrates" [MeSH Terms:noexp] OR "amphibians" [MeSH Terms] OR "birds" [MeSH Terms] OR "fishes" [MeSH Terms] OR "reptiles" [MeSH Terms] OR "mammals" [MeSH Terms:noexp] OR "primates" [MeSH Terms:noexp] OR "artiodactyla" [MeSH Terms] OR "carnivora" [MeSH Terms] OR "cetacea" [MeSH Terms] OR "chiroptera" [MeSH Terms] OR "elephants" [MeSH Terms] OR "hyraxes" [MeSH Terms] OR "insectivora" [MeSH Terms] OR "lagomorpha" [MeSH Terms] OR "marsupialia" [MeSH Terms] OR "monotremata" [MeSH Terms] OR "perissodactyla" [MeSH Terms] OR "rodentia" [MeSH Terms] OR "scandentia" [MeSH Terms] OR "sirenia" [MeSH Terms] OR "xenarthra" [MeSH Terms] OR "haplorhini" [MeSH Terms:noexp] OR "strepsirhini" [MeSH Terms] OR "platyrrhini" [MeSH Terms] OR "tarsii" [MeSH Terms] OR "catarrhini" [MeSH Terms:noexp] OR "cercopithecidae" [MeSH Terms] OR "hylobatidae" [MeSH Terms] OR "hominidae" [MeSH Terms:noexp] OR "gorilla gorilla" [MeSH Terms] OR "pan paniscus" [MeSH Terms] OR "pan troglodytes" [MeSH Terms] OR "pongo pygmaeus" [MeSH Terms]) OR ((animals[tiab] OR animal[tiab] OR mice[Tiab] OR mus[Tiab] OR mouse[Tiab] OR murine[Tiab] OR woodmouse[tiab] OR rats[Tiab] OR rat[Tiab] OR murinae[Tiab] OR muridae[Tiab] OR cottonrat[tiab] OR cottonrats[tiab] OR hamster[tiab] OR hamsters[tiab] OR cricetinae[tiab] OR rodentia[Tiab] OR rodent[Tiab] OR rodents[Tiab] OR pigs[Tiab] OR pig[Tiab] OR swine[tiab] OR swines[tiab] OR piglets[tiab] OR piglet[tiab] OR boar[tiab] OR boars[tiab] OR "sus scrofa"[tiab] OR

...to ensure that you access recent papers also, not just the ones that have been indexed. Relatively few papers are indexed with 3R MESH terms in MEDLINE



Transgenic AND Mice (grey)



Transgenic OR Mice (everything)



Transgenic NOT Mice (black)

Transgenic AND (mice OR rats OR (pigs NOT guinea))

protection NEAR animals NEAR scientific

The EURL ECVAM Search Guide

Can be ordered free of charge from

bookshop.europa.eu



Contents

- Data sheets on
 - Journals
 - Databases
 - Meta-databases
 - Database hosts
 - Open Access resources
 - Organisations
 - Web search engines



Contents

<text><section-header>

- Data Retrieval Procedures (basic principles)
- Check-list for searching for information on alternative methods
- · Tables comparing the features of
 - Databases
 - Journals
 - Organisations




Seven Golden Steps to Successful Searching

- 1. Clearly define and be aware of your specific information need
- 2. Identify the fundamental components of your scientific approach
- 3. Choose the most appropriate information resources
- 4. Compile relevant and necessary search terms
- 5. Start your search with a simple query in a 3Rs specific context
- 6. Limit search results from more extensive resources
- 7. Broaden the search horizon

Archive your searches and the key documents

- Avoidance of repeating searches
- Documentation of searches
- Generation of bibliographies for publications
- Search function

The world congresses on the 3Rs are important 3Rdrivers and disseminators of information: 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



Examples of 3R sources

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

National 3Rs Centres



www.nc3rs.org.uk

Centres giving information on alternatives





University of California Center for Animal Alternatives



www.lib.ucdavis.edu/dept/animalalternatives



Animal Welfare Information Center

U.S. DEPARTMENT OF AGRICULTURE NATIONAL AGRICULTURAL LIBRARY

awic.nal.usda.gov

Animal welfare organisations

Reducing suffering - Rabbit welfare

Dack to research animals home

AND ADVICE

0300 1234



RSPCA

Campaigns

Animal Care

\$



My RSPCA Help



Refining rabbit care A resource for those working with rabbits in research

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 quidance on refining laboratory rabbit husbandry





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



www.rspca.org.uk/sciencegroup/researchanimals

more Refinement

introduction





For as long as animals are used in

Reducing suffering:

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

Three Rs Search Guide

If you plan to use animals for scientific purposes, you must complete an animal use protocol and submit it to animal an care committee for approval prior commencement of the to study. The animal use protocol outlines how the Three Rs will be the implemented in animal-based proposed procedures. To find the most up-to-date information the Three Rs, on investigators typically conduct structured а search. information 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 <u>Step-by-Step Three Rs</u> <u>Search Strategy</u>.

Journals

ATLA (Alternatives to Laboratory Animals) Animal Welfare (UFAW) ILAR Journal Laboratory Animals Comparative Medicine

See http://norecopa.no/other-resources/journals for more

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



http://ilarjournal.oxfordjournals.org

Guidelines as a source of 3R resources

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:

https://norecopa.no/3r-guide-database

Search 3R Guide 🛛 🕐	
Find 3R resources	
1	- All Categories -
	Agricultural animals
	Anaesthesia and analgesia
	Aquatic animals
	Behavioural research
	Birds
	Blood sampling
	Cancer research
	Design
	Disease research
	Education and training
	Environmental enrichment
	Ethics & harm-benefit analysis
	Fish
	Handling
	Housing and management
	Humane killing
	Miscellaneous
	Neuroscience research
	Non-human primates
	Nutritional research
	Procedures
	Reporting
	Surgical research
	Toxicology
	Transport
	Wildlife

Email discussion groups

e.g. CompMed + archive LAREF VOLE Norwegian forum for contact persons

See https://norecopa.no/other-resources/emaildiscussion-lists for more Documentation of a search for alternatives is required by Norwegian law when applying for permission to conduct animal experiments, and it is *your* responsibility!

AJ Smith & T Allen, 2005

The use of Databases, Information Centres and Guidelines when planning research that may involve animals Animal Welfare, 14 (4): 347-359

http://oslovet.norecopa.no/SmithAllen.pdf







Search strategies in a nutshell

- Define the search as well as possible
- Identify synonyms and 3R terms
- Remember the differences between British & American English
- Use several databases (little overlapping)
- Learn the differences between the search engines (read the instructions!)
- Get used to using Boolean logic and check which terms are supported by the search engine
- Learn how to expand/narrow your search
- Look for core articles and key authors
- Use the possibilities on the Internet to get in touch with the best research labs

colourbox.com

EARLY PLANNING FOR A PROJECT WHICH MIGHT INVOLVE THE USE OF ANIMALS

Scientists using animals in scientific procedures have an ethical and legal obligation to ensure that the Three Rs, namely Reduction, Refinement and Replacement, are implemented wherever possible. This strategy was designed by the Focus on Ademptives' group to help scientists meet this obligation. The strategy should be applied at the beginning of a project, and at regular intervals throughout. Advice should be sought from the Ethical Review Process and Home Office inspectorate.



"Userdoorship of this Fosce on Adversatives controllines includes the DE Hadreen Toud, TRAME, The Nemerann Possearch Tout, The Load Doording Fand, PSPCA, SLAndree Animal Fund and UFAP. Copies of the poster are ablamable bein FRAME, 96-98 North Shervood Steat, Notingham, NGL 461. Tel 0115 198 4240. Faic 0115 998 3320. Lengt hanne@themic.org.uk.

Focus on Alternatives (FoA)

A consortium of UK animal welfare organisations

https://norecopa.no/media/6 663/earlyplanningposter.pdf and https://norecopa.no/media/6 672/investigationposter.pdf

Norecopa

National Consensus Platform for the Replacement, Reduction and Refinement of Animal Experiments



European Consensus-Platform for Alternatives

www.ecopa.eu



- Following an initiative at the 3rd World Congress on Alternatives and Animal Use, Bologna 1999
- Established in 2000
- National Consensus Platforms (NCPs) with all 4 stakeholders equally represented:



The organisation is registered in Brønnøysund with

- statutes
- its own Board
- Annual General Meeting as the highest organ
- secretariat (50% position) attached to the Norwegian Veterinary Institute

Norecopa's budget from the State for 2016 is NOK 1.300.000,-In addition: members fees (NOK 200/1000,- per year).

International consensus meetings

Harmonisation of the Care and Use of: Fish (2005) Wildlife (2008) Fish (2009) Agricultural animals (2012)

http://norecopa.no/meetings

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



Expert Working Group report on severity classification

Conducted in support of the revision of Directive 86/609/EEC on the protection of animals used for

section and the hold fraction fraction & 610 fraction. Fraction (1) 5,201 fr

B-1049 Bruxelles / Europese Commissie, B-1049 Brussel - Belolum, Telephone: (32-2) 299 11 11

Expert working group on severity classification of scientific procedures performed on animals

FINAL REPORT Brussels, July 2009

angije hotbanar monoran za selihano ao am i

scientific purposes

http://ec.europa.eu/environment/chemicals/lab_animals/pdf/report_ewg.pdf

Published online on 9 May 2011 Lab Anim, doi: 10.1258/a.2011.010181

Working Party Report

Guidance on the severity classification of scientific procedures involving fish: report of a Working Group appointed by the Norwegian Consensus-Platform for the Replacement, Reduction and Refinement of animal experiments (Norecopa)

P Hawkins (Convenor)¹, N Dennison², G Goodman³, S Hetherington⁴, S Llywelyn-Jones⁵, K Ryder² and A J Smith⁶

¹Research Animals Department, REFCA, Wibenforce Way, Southwister, West Susses: Re13 965, UK, ²Animals Glorente Tencodares) Impactosite, Humo Ottore, PIG 666 1672 Duride DOI 194W. UK, ²Holingioui Savicea, Jine University of Editubuth, Charnelofo Ruiking, 49, Libe France Crescent, Editourgh EHH 458, UK, ³CEFAS, Palefield Road, Lowelt dt, NR38 047, UK, ³Moracoga, o/o Norwegian Velantary Biological Services Unit, 4th Root, Hodgin Building, Guly's Campus, London SE1 114, UK, ⁵Moracoga, o/o Norwegian Velantary Institute, PD Box 750 Services, Fability David Mediteppozory, k

Abstract

The severity classification of procedues using animals is an important tool is help focus the implementation or infinement and to assist in exporting the application of the BRs (explacement, enduction and refinement). The recently invited Directive that regulates animal research and lesting within the European Union requires Member States to ensure that all procedures are classified as "non-recovery", "mild", "modentir or 'severe', using assignment criteria set out by the European Commission (EC). However, these are focused upon temestrist species, so are of limited releaves to the states. However, and upon electric the BRs (Nonecopa) has produced guidance on the classification of severity in scientific procedures involving this, including examples of 'subthenbolt', mild', "modentir, "several and "upon threshild minimate. Nonecopa has established a website (www.nonecopa.no/categories) where more information on severity classification for procedures using this, including response on the several and severity in classification of procedures using their, including response on the several and severity classification of procedures using their, including response on the several and severity classification of procedures. The several and severity classification of procedures using their, including response on the several and severity classification of procedures using their, including response on the several and severity classification of procedures using their, including response on the several and severity classification of procedures using their including their desame in which we may maintain the severity in the severity in the severity in the severity classification of procedures using the including their desame in the severity classification of procedures using their including their desame in the severity classification for the severity in the severity classification of the severity classification of the severity in the severity classification and the severity classification the severity in the

Keywords: Fish, harm-benefit assessment, humane endpoints, refinement, severity

Laboratory Animats 2011: 1-6. DOI: 10.1258/la.2011.010181

Background

An effective prediction of the effects of a research protocol on the animalic concerned heips to ensure that any pain, suifering or distess they may experience will be effectively articipated, recognized and alleviated. This is essential not because physical and behavioural responses to suffering can significantly affect data quality. Severity classification is thus an important tool to help focus the implementation of refinement, including monitoring its progress, and to assist in reporting the application of the 3Rs (eplacement, including nonitoring, its new an independent) hurch, 'which is new an independent of the Regislation on animal research and toting in many countries. Predictions of severity are also fundamental to the harm-bendit

assessments undertaken by bodies such as negulatory authorities and ethical committees when deciding whether or not a project should be licensed or funded. There may also be a legal requirement to predict and clas-

sity severity. For example, the new Directive regulating animal use writhin the European Uhica, which must be implemented within all Member States by January 2013, requires the severity of each procedure to be classified on the basis of the dagree of pair, suffering, distress or latting harm expected to be experismed by an individual animal during the course of the procedure, with the aim of enhancing tinnsparency, facilitating the project authorization process and providing tools for monitoring compliance.² Member States will have to ensure that all procedures are desailed as 'non-recovery', 'mild', 'modeated or 'severe' on a case-by-case basis, using the assignment

Laboratory Animais 2011: 1-8

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More (species- and situation-) specific guidance may be necessary to implement the 3Rs

Guidance on the severity classification of procedures involving fish

Report from a Working Group convened by Norecopa

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

Laboratory Animals, 45: 219-224, 2011





Organisations of relevance to animal research

Organisations within Laboratory Animal Science

AAALAC International 🔀 (Association for Assessment and Accreditation of Laboratory Animal

Care International)

AALAS 🔀 (American Association for Laboratory Animal Science)

ACLAM C (American College of Laboratory Animal Medicine)

AniMatch 📝 (an online sharing platform for the exchange of organs and tissues)

ARSAL 🛃 (Asociatia Româna pentru Stiinta Animalelor de Laborator; Romanian Laboratory Animal

Science Association)

ASLAP 🛃 (American Society of Laboratory Animal Practitioners)



Norecopa promotes use of "The Three Rs":



Norecopa aims for consensus between the four stakeholders:

Government and Regulatory Authorities - Research and teaching - Industry - Animal protection and welfare

Who are you?

Are you a researcher, student or are you generally interested in animal welfare? Here you will find relevant information to help you achieve your goals.



Contact oss

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Org.no. 992 199 199 Bank account: 7694 05 12030 (IBAN: NO51 7694 0512 030) (payment must be marked '12025 Norecopa')

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- > Give us some feedback!
- > 2010/63/EU
- > Information material
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Norges miljø- og biovitenskapelige universitet



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Jerry K-9 CPR Mannikin (Dog)

 Record number:
 8821 (legacy id: 4905)

 Category:
 Handling (TextBase) - Medicine

 Type:
 Simulator

A product line of animal CPR (Cardiopulmonary Resuscitation) training mannequins. Type: Simulator. Category: Handling & Veterinary Medicine.

Jerry K-9 CPR Mannikin is a full size dog for CPR

(Cardiopulmonary Resuscitation) training. Features: Working lungs, artificial pulse, disposable and cleanable parts. Designed to perform CPR compressions, mouth-to-snout resuscitation. Also designed to splint and bandage. In addition, a non-removable, long oblique fracture of the right femoral leg bone can now be added to this mannikin. This will allow students to learn how to set and repair common K-



9 fractures. This mannikin simulates a 60-70 lbs dog. Accessories included: Carrying case with kneeling pad, brush, 5 disposable lungs. This mannikin is a simplified version of <u>Critical Care</u> Jerry.

Comments & References: Additional Disposable Lungs for Jerry: 24 disposable lungs: US\$128.00; 72 disposable lungs: US\$380.00. Suitable for training in the veterinary setting, search and rescue, veterinary schools, canine units and for pet owners. This item may be borrowed for up to 6 weeks through the Alternatives Loan System of the International Network for Humane Education (InterNICHE), free of charge, but return postage must be paid by the person who has borrowed the product. Please note that there are practical limitations on where some items can be sent. For more information, please contact <u>loansystem@interniche.org</u>. See also http://www.interniche.org for more information.

Item: 101

Price: US\$989.00. Loan Program: Free of charge Free of charge: Loan Program: Free of charge

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The search engine



- An index of all the words on all the approx. 6,300 pages
- Fuzzy logic
- Boolean logic
- Wildcards
- Proximity searches
- Truncation
 - A help file available



United States Department of Agriculture

Collaboration with US Department of Agriculture

Search for 'bleeding mice' on Google and Norecopa.

bleeding mice

of Mice and Rats

3R Guide/10891

bleeding mice

Images

All

Videos Search all Norecopa's databases and webpages simultaneously:

Q

Q

About 4,760,000 results (0.3 Welcome to Norecopa's new website! (PDF) Methods of Bloo Search engine help file www.osa.sunysb.edu/dlar

More about Norecopa's databases: 3R Guide - NORINA - TextBase - Classic AVs

Collecting blood from mice number of efficient methods

(PDF) Guidelines for S oacu.od.nih.gov/ARAC/dc Guidelines for Survival Blee investigators and National I

Blood sample collec www.ncbi.nlm.nih.gov > N

by S Parasuraman - 2010 -It is important that blood sa (NIH) Animal Care and Use Committees (ACUC) in their choice and application of survival rodent This method is recommended bleeding techniques.

How to obtain blood



Blood sampling Blood sampling is one of the commonest procedures conducted on research animals, but it may See m ; cause pain, distress and lasting harm if the technique is poor, or if too much of the circulating blood volume is removed. Videos and slide series showing blood sampling techniques on several common laboratory animal speciesLinks NC3Rs Microsite on blood sampling Films and slide shows on bleeding techniques...

76 results

NIH Animal Research Advisory Committee Guidelines for Survival Bleeding

These guidelines have been developed to assist investigators and National Institutes of Health

[PDF] A rapid, simple, ceua.ufsc.br/files/2010/06 Methods for obtaining bloor

Mouse : Decision tre bodyweight. A mouse weigh Veterinary Medicine

that allows investigators to i Blood Collection in Mice Using the Saphenous Vein - An Alternative to **Retro Orbital Collection**

NORINA/8641

https://www.nc3rs.org.uk/ These web pages describe a method for blood collection from the saphenous vein of mice, rats, How much blood does a m, hamsters, gerbils, guinea-pigs, mink and ferrets. Type of record: Web pages. Category:

Search filters Order by: Relevance Enable synonyms and stemming 0 Browse the databases eBooks (6) Free (5) Held at NMBU Oslo (contact kristine.hansen@nmbu.nol (5) Key products (6) On loan (2) Reviewed Θ Database 3R Guide (6) Classic AVs (6) Website (6) NORINA (35) TextBase (23) • Search in the databases / All Text Title

Author

Publisher



Newsletter 8-9 times a year

- something for you?



Dette brevet inneholder følgende saker:

- Nå er det på tide å nominere til 3R-prisen!
- Nye nettsider for Norecopa
- · Arbeidsseminar om design og statistikk
- Frist for sammendrag til FELASA
- Nettbasert kurs om sebrafisk
- · Ny modul om dyrevelferd fra Newcastle
- Forbedring av fiskeforsøk
- · Rådet for dyreetikk har fått nye medlemmer
- Nyheter fra 3R-sentre og komitéer
- UiB-nettside om 3R
- Glimt fra forskningen
- · Merking av vilt
- Registrering av smerte hos sau
- 3R-fremskritt i tidsskriftet Laboratory Animals
- Nytenkning premieres
- Åpenhet rundt dyreforsøk
- Til ettertanke
- Estimatione
- Møtekalenderen (oppdatert)







Norecopa's 3R prize (30,000 kroner + diploma)

Deadline for nominations: 15 March

Newsletter 8-9 times a year

- something for you?



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