A Practical Guide to Planning, Conducting and Reporting Animal Studies

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@adrian_3r

norecopa.no/NRW

https://norecopa.no

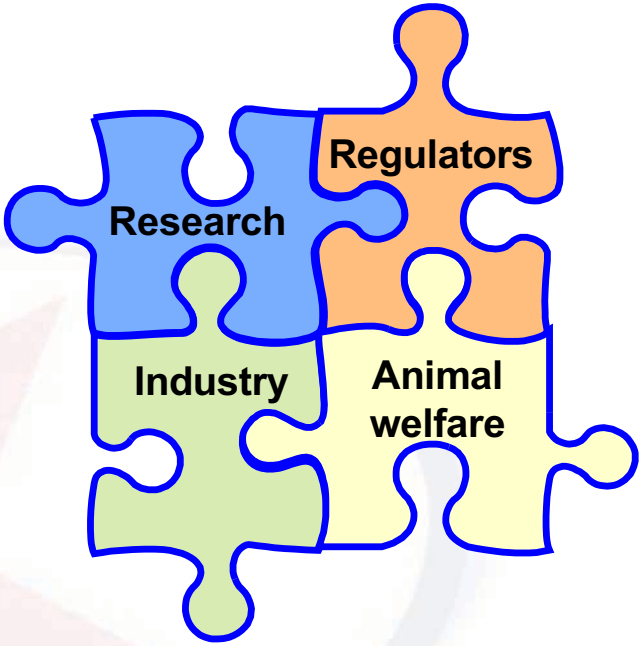
Norecopa: PREPARE for better Science

Norecopa is Norway's National *Consensus*-platform,

working to advance ***all the three R's***:

Replacement, Reduction and Refinement

Its Board represents:



Established in 2007

Norecopa: PREPARE for better Science

norecopa.no

norecopa.no/global3r

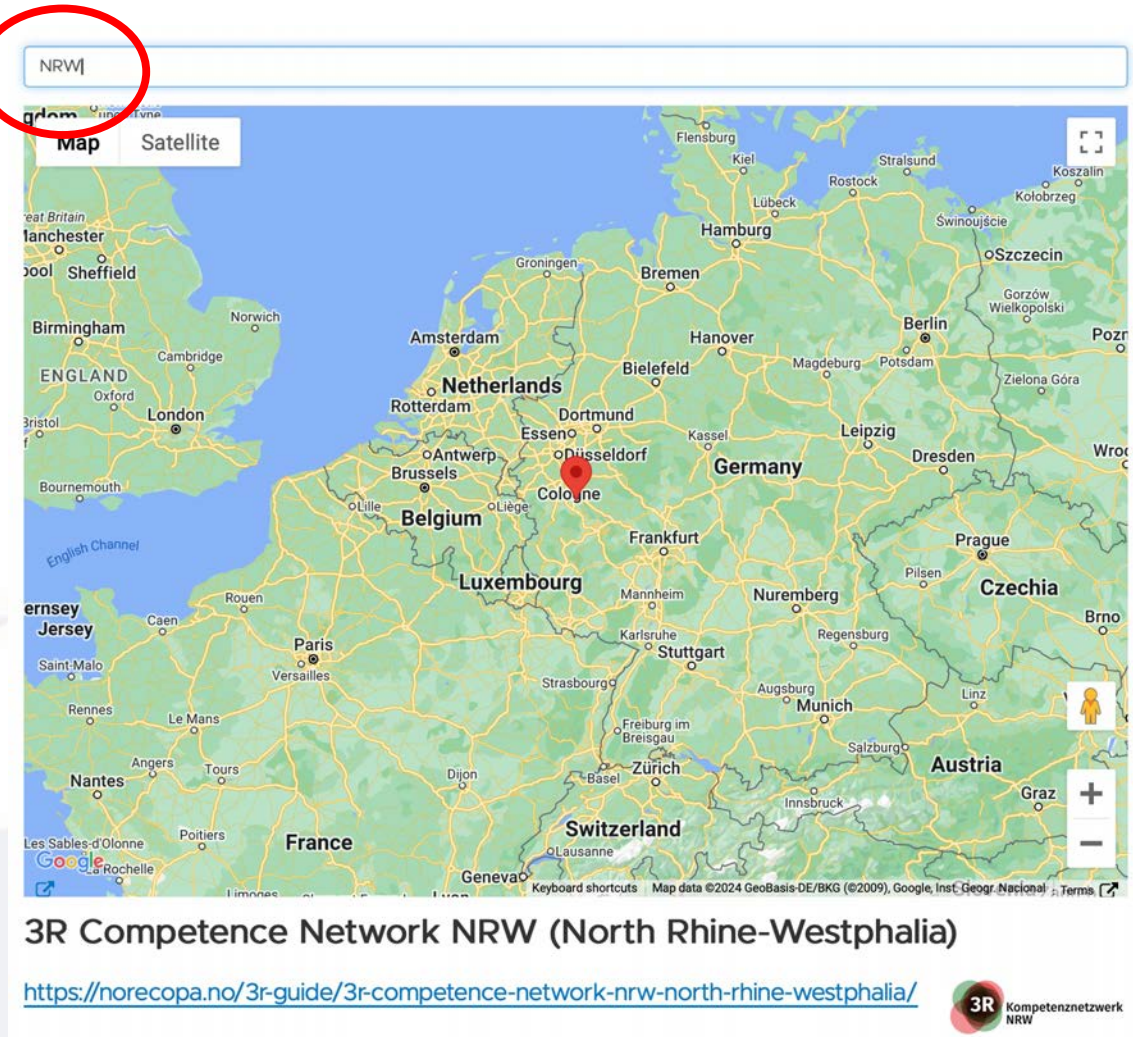
EU3Rnet, a network of 3R centres: norecopa.no/3r-guide/eu3rnet

Centres

- Replacement
- Reduction
- Refinement
- ecopa

Associations

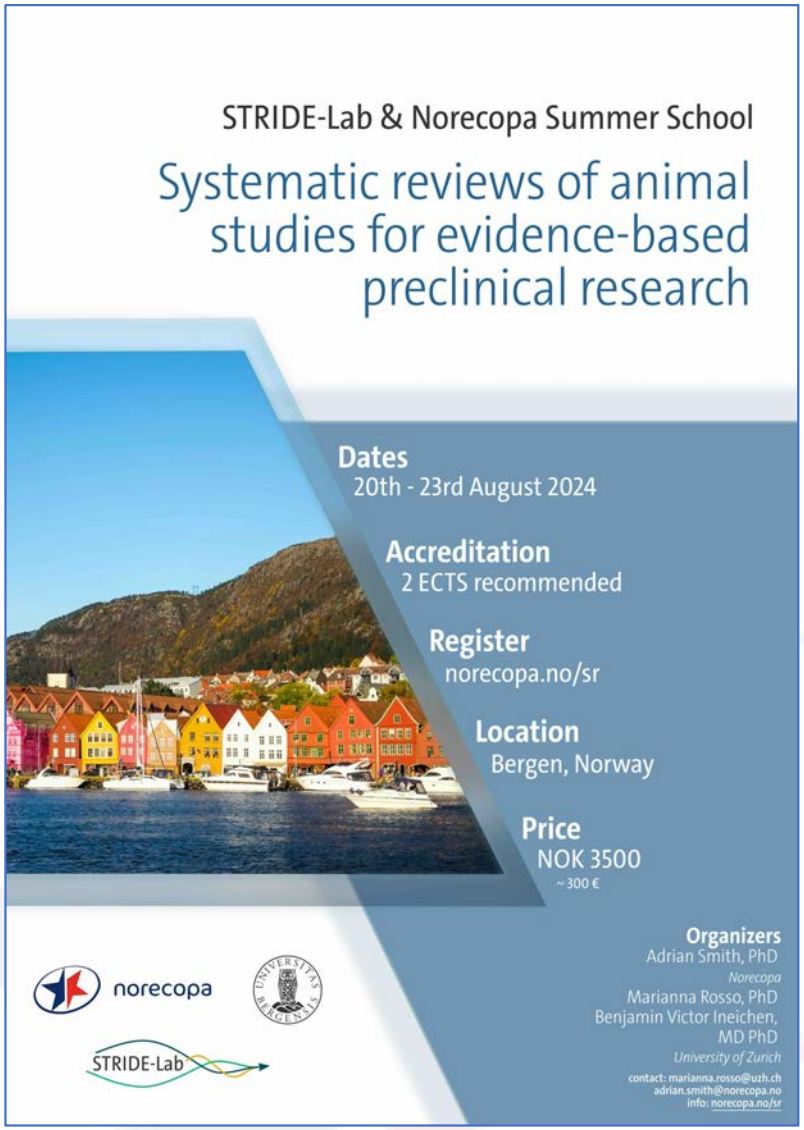
- ACURET
- AFLAS (includes South Korea)
- Culture of Care Network
- ecopa
- EU-NETVAL
- EU3Rnet
- FELASA
- FESSACAL
- Scand-LAS
- Concordat on Openness



3R Competence Network NRW (North Rhine-Westphalia)

https://norecopa.no/3r-guide/3r-competence-network-nrw-north-rhine-westphalia/

3R Kompetenznetzwerk NRW



Norecopa: PREPARE for better Science

Calling early career researchers !

More information:
https://norecopa.no/SR

”better Science?"

- replacement if possible
- reduction and refinement if not possible to replace
- valid data (a true treatment effect)
- reproducible and translatable experiments
- best possible animal welfare
- health & safety (of animals and people)
- a culture of care at the animal facility
- communication of best practice to others

colourbox.com

https://norecopa.no/prepare-care-share-flag

'Our long experience and modern coffee machines are your guarantee of quality' (?)

norecopa.no : an updated overview of global 3R resources

over 10,000 webpages
approx. 1,000 hits daily

7-8 detailed newsletters per year

May 2024

- Contemporary debates in biomedical ethics - How to write an essay in bioethics, Basel, 6 May 202
- A Practical Guide to Planning, Conducting and Reporting Animal Experiments, webinar (Adrian Smith), 7 May 2024
- Severity assessment in preclinical psychiatry research, webinar (Anne Mallien), 7 May 2024
- Responsibility as linchpin of animal experimentation ethics, webinar (Stef Aerts), 8 May 2024
- 8th Annual Meeting of AWRN (Animal Welfare Research Network), Belfast, 8-9 May 2024
- Meeting the Information Requirements of the US Animal Welfare Act, online workshop, 8-9 May 2024
- Charles River/Jackson Laboratory Seminar on Colony Management, Diet and Immune-Humanization, Copenhagen, 13 May 2024
- Beyond the 3Rs: How can we change the animal research paradigm?, Basel/online (Kathrin Herrmann), 13 May 2024
- ReThink 3R workshop, Berlin, 13-14 May 2024
- Health and Management of Zebrafish in Research,
- Colony management, dietary considerations and mou
- Anaesthesia and Perioperative Care of Laboratory R
- Wild Animal Welfare Committee (WWAC) Conference - Translating wildlife welfare into practice: wildlife management in the 21st century, online, 16 May 2024
- COLAAB Workshop to Explore Animal Methods Bias in Biomedical Research Funding, online, 16 May 2024
- Guidelines for the establishment and functioning of Animal Ethics Committees (Institutional Animal care and Use Committ in Africa, PAN-LASE/ICLAS webinar, 16 May 2024
- Clickertraining zur Stressreduktion bei Schweinen im Versuchsalltag, webinar (Jennif
- Reliability of Research Data - A Workshop for Young Scientists
- Scand-LAS, Tampere, 21-24 May 2024
- The 3R Länd: Towards the Futur search with Organoid, Organ-on-Chip and In Silico Models, Tübingen, 21-2
- 22-24 May 2024
- new 3R opportunities and create a project? Swiss 3RCC Early Career Researcher Network hackathon, 23 May
- Organ-on-chip workshop, Jena, 27-29 May 2024
- Introduction to microbiological monitoring in rodents facilities, online FGB event (discount if also attending this course), 29 May 2024
- The use of anaesthesia in laboratory rodents, webinar (Henri Bertrand), 29 May 2024
- UK Animal Law Conference 2024, Birmingham, 29-30 May 2024
- Development and validation of test methods, Swedish 3Rs Center webinar (Kristina Fant), 30 May 2024
- Summer Immersion on Innovative Approaches in Science, Washington D.C., 30 May - 1 June 2024
- Fish as experimental animals - zebrafish CRISPR and in vivo imaging, Copenhagen/online, 30 May - 7 June 2024

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norecopa.no/meetings/meetings-calendar

+ webpages for recorded meetings, sorted by PREPARE topics

40-slide powerpoint presentation about the 3Rs

ccac.ca

The 3Rs of Russell and Burch:

Replacement, Reduction & Refinement

Available at norecopa.no/3Rs

With some material from:
Smith AJ & Richmond J (2024). The Three-Rs.
In: *The UFAW Handbook on the Care and Management of Laboratory and Other Research Animals.* 9th edition.
Richardson CA and Golledge HDR (eds).
Oxford: Wiley-Blackwell.

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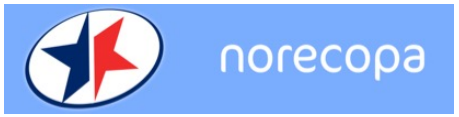

norecopa.no/3Rs

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Direct / contingent inhumanity

Russell and Burch distinguished between

- direct inhumanity: the pain or distress of a procedure (even when performed perfectly)
  e.g. pain of injection, immobilisation stress

- contingent inhumanity: the side-effects of a procedure that are not necessary for its success
  e.g. poor transport, housing, care, handling, substance administration, bloodsampling, anaesthesia, analgesia and killing

colourbox.com

Pain and suffering is experienced at the level of the individual

Harm-Benefit Analysis

- ***The harm*** is experienced **NOW, and is certain**
- **The benefit** is ***in the future***, for ***other animals or humans***, and ***is uncertain***
- HBA analysis is meaningless if the data from the experiment are unreliable
- So we need ***guidelines*** both ***for HBA*** and for ***experimental design & statistical analysis***

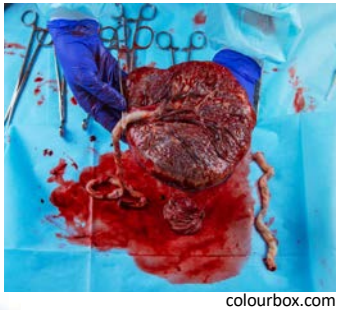
norecopa.no/concerns

NAMs og NATs

NAMs: New Approach Methodologies (not *Non-Animal Methods!*)

Avoidance (methods which don't directly replace animal experiments)

e.g. studies on the human placenta
"Read-Across"


colourbox.com

	Chemical 1	Chemical 2	Chemical 3	Chemical 4
Structure	xxxxxxxxx	xxxxxxxxx	xxxxxxxxx	xxxxxxxxx
Property 1	● ⇨ ○		● ⇨ ○	
Property 2	● ⇨ ○		○ ⇦ ●	
Property 3	○ ⇦ ●		● ⇨ ○	
Activity 1	● ⇨ ○		● ⇨ ○	
Activity 2	● ⇨ ○		○ ⇦ ●	
Activity 3	○ ⇦ ●		● ⇨ ○	

● Existing data point ○ Missing data point

NATs: Non-Animal Technologies

Alternatives to animal experiments

e.g. organoids (mini-organs)
organs-on-chips
experiments on fruit flies

NB. Those who work with NAMs may not even be aware that they use a method that can reduce animal use.
It is therefore important to build bridges between the lab animal community and the NAMs/NATs-communities !

https://www.oecd.org/chemicalsafety/risk-assessment/groupingofchemicalschemicalcategoriesandread-across.htm

https://nc3rs.org.uk/sites/default/files/documents/NonAnimalTechCO082_RYE_4_nrfinal2.pdf

Disclosures about resources which will be mentioned

- *Webmaster for the Norecopa site - information about global guidelines*
- *Lead author of several databases on the Norecopa site*
- *Lead author of the PREPARE guidelines*
- *Manager of the Refinement Wiki*
- *Norecopa is a member of AAALAC International but receives no financial support*

My starting point when trying to improve science

- Manager of an old facility with suboptimal standard while lecturing on good Laboratory Animal Science
- The most traumatic memories concerning poor practice were related to facility issues, not weak experimental design
- We sought (and obtained) accreditation from AAALAC International to bring the facility up to standard
- There were few good overviews of guidelines on how to conduct better science, so we started to produce our own overviews

Dagbladet.no Publisert fredag 23.04.2010 kl. 18:26

Solveig (38) forsket på kreft, ble selv uhelbredelig syk

Slår alarm om arbeidsforholdene på Radiumhospitalet. Sykehuset innrømmer rutinesvikt.

ASLE HANSEN ash@dagbladet.no

DIANA BADI dba@dagbladet.no

HELSEFARLIG ARBEIDSMILJØ: Solveig Garman-Vik (38) har fått diagnosen akutt myelogen leukemi (AML) etter å ha jobbet med kreftforskning på Radiumhospitalet i elleve år. Her får hun en klem av sykepleier Elisabeth A. Saghaug før hun går hjem for helgen. Få med hvor fantastiske alle her på Lovisenberg er mot meg, sier Solveig. Foto: LARS EIVIND BONES/DAGBLADET

The Burnt Cake Fallacy

We cannot improve our research by

better reporting alone...

we need reporting **and** planning guidelines

reddit.com

The pathway to open (better) science

Norecopa: PREPARE for better Science

https://riojournal.com/article/105198

norecopa

Reporting guidelines like ARRIVE describe the experiment. Guidelines like PREPARE are used to plan the experiment (choose the «ingredients» and «baking time»)

marksandspencer.com

Guidelines for specification of animals and husbandry methods when reporting the results of animal experiments

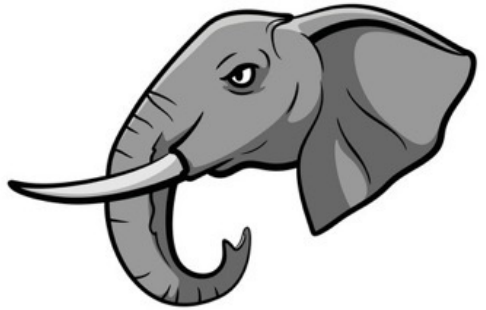
WORKING COMMITTEE FOR THE BIOLOGICAL CHARACTERIZATION OF LABORATORY ANIMALS/GV-SOLAS
Chairman: Dr A. W. Ellery, c/o Solco Basle Ltd, Rührbergstrasse 21, CH-4127 Birsfelden, Switzerland

- Ellery (GV-SOLAS), 1985
- Öbrink & Waller, 1996
- Reporting animal use in scientific papers (Jane Smith *et al.)*, 1997
- Öbrink & Rehbinder: Animal definition: a necessity for the validity of animal experiments? *Laboratory Animals,* 2000
- Guidelines for reporting the results of experiments on fish (2000)
- ARRIVE Guidelines, 2010 (Kilkenny *et al.*, NC3Rs), updated in 2020
- Gold Standard Publication Checklist, 2010 (SYRCLE)
- Institute for Laboratory Animal Research, NRC, 2011
- Instructions to authors, in many journals

The elephants in the room…

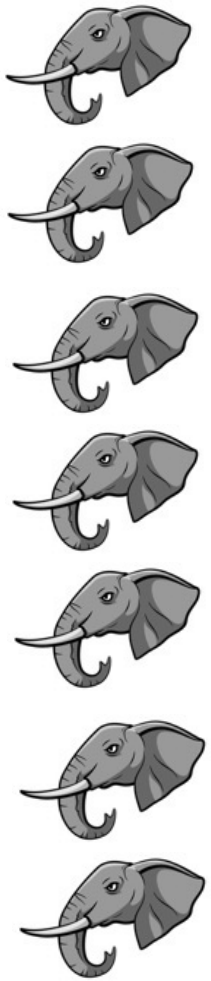
reddit.com

…the largest of them all is inadequate attention to detail during planning of animal studies, including collaboration with the animal facility from day one



Some of the elephants...

- poor literature searches
- lack of humane endpoints
- poor study design, including choice of procedures
- vague distribution of work and costs between the scientists and the animal facility
- insufficient evaluation of the facility's competence and infrastructure
- too little attention to transport and acclimation
- ignoring health risks for all involved
- lack of standard procedures for necropsy
- poor planning of waste disposal
- little discussion about the fate of the animals



We have tried to solve the “reproducibility crisis” for many years

Hurni 1969

(cited by Waller & Öbrink, 1996)

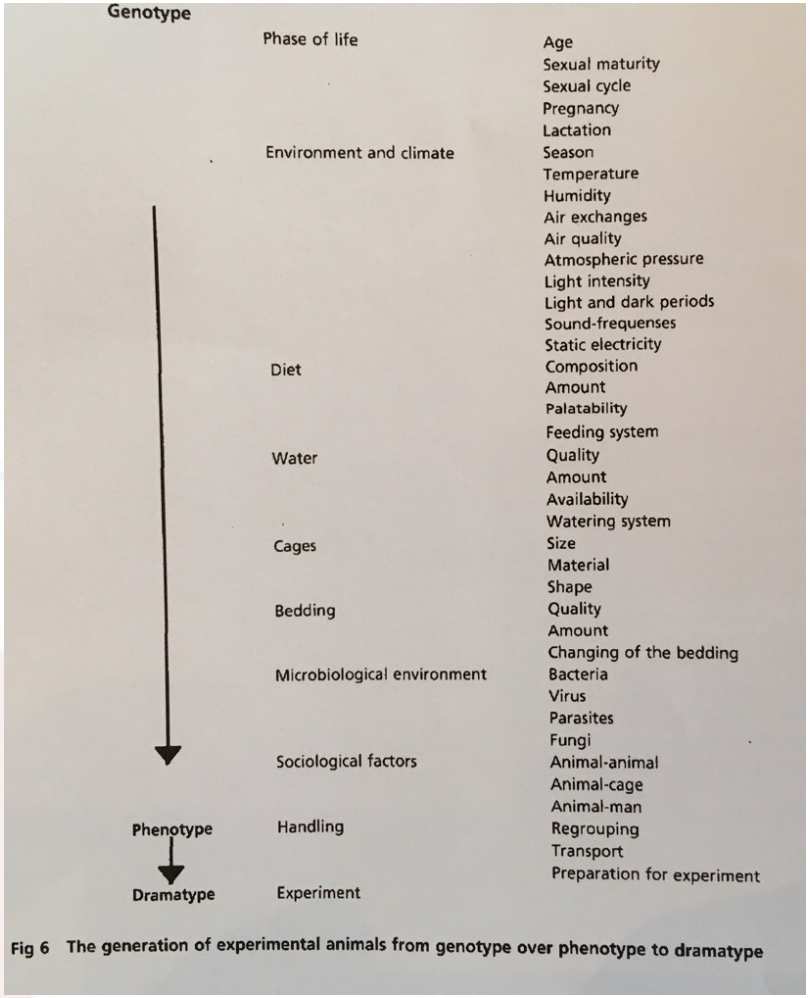
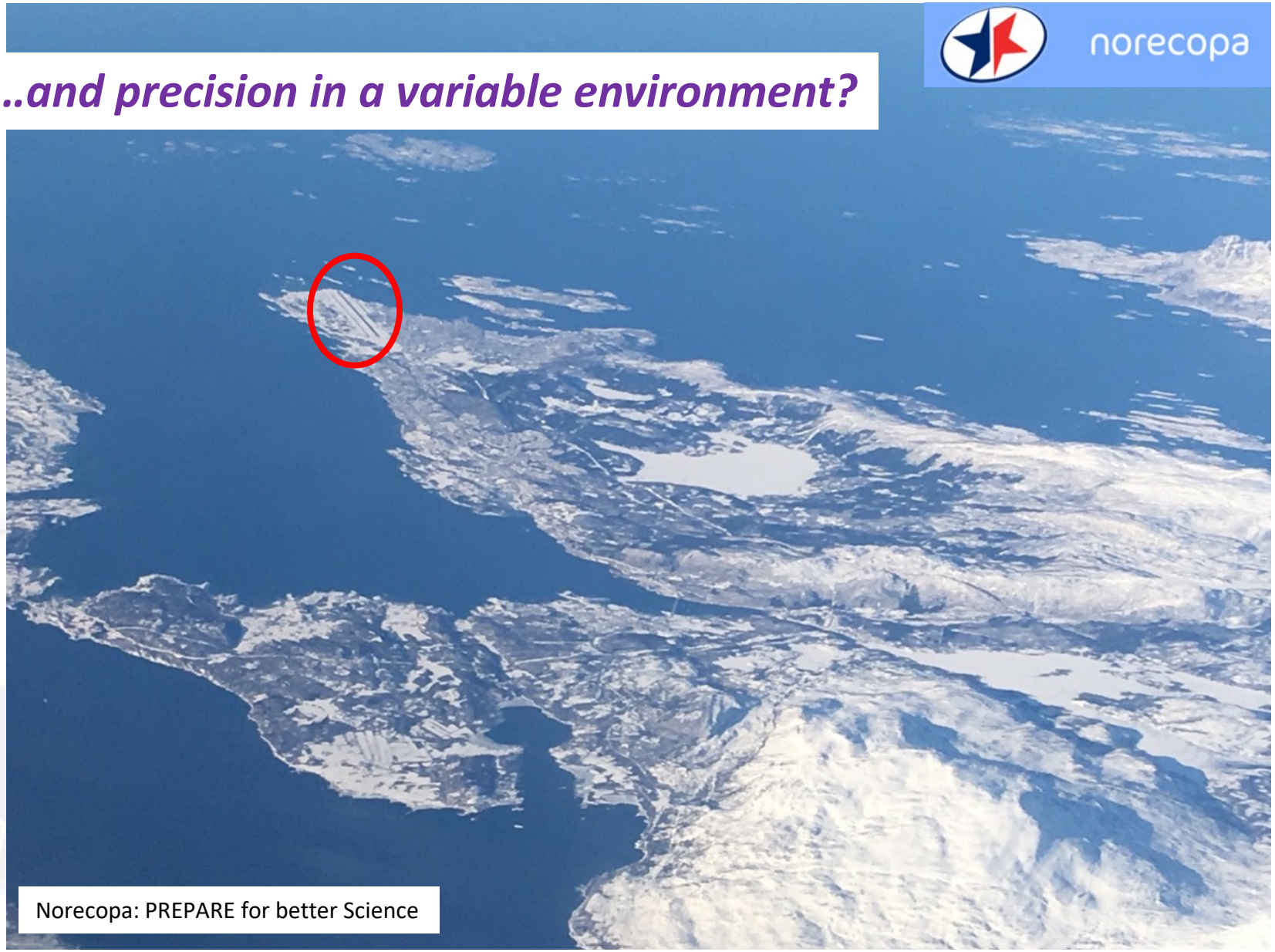


Fig 6 The generation of experimental animals from genotype over phenotype to dramatype

How do others achieve success and reproducibility?

https://www.meonuk.com/runway-markings-explained

…and precision in a variable environment?



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travelandleisure.com/airlines-airports/what-happens-when-planes-hit-birds

15.25.33	-01.38	Kaptein	Cockpit	V one, rotate
15.25.38	-01.33	Kaptein	Cockpit	positive rate
15.25.39	-01.32	Styrmann	Cockpit	Gear up please
15.25.39	-01.32	Kaptein	Cockpit	Gear up
15.26.37	-00.34	Kaptein	Cockpit	Uh what a view of the Hudson today
15.26.42	-00.29	Styrmann	Cockpit	Yeah
15.27.07	-00.04	Kaptein	Cockpit	After takeoff checklist complete
15.27.10	-00.01	Kaptein	Cockpit	Birds
15.27.11	-00.00	Styrmann	Cockpit	Whoa
15.27.11	00.00			
15.27.12	+00.01	Kaptein	Cockpit	Oh ---
15.27.13	+00.02	Styrmann	Cockpit	Oh yeah
15.27.14	+00.03	Styrmann	Cockpit	Uh oh
15.27.15	+00.04	Kaptein	Cockpit	We got one rol... both of 'em rolling back
15.27.18	+00.07	Kaptein	Cockpit	Ignition, start
15.27.21	+00.10	Kaptein	Cockpit	I'm starting the APU
15.27.23	+00.12	Kaptein	Cockpit	My aircraft
15.27.24	+00.13	Styrmann	Cockpit	Your aircraft
15.27.28	+00.17	Kaptein	Cockpit	Get the QRH... loss of thrust on both engines
15.27.32	+00.21	Kaptein	Radio	Mayday mayday mayday. Uh this is Cactus fifteen thirty [sic] nine, hit birds. We've lost thrust on both engines. We're turning back towards LaGuardia.

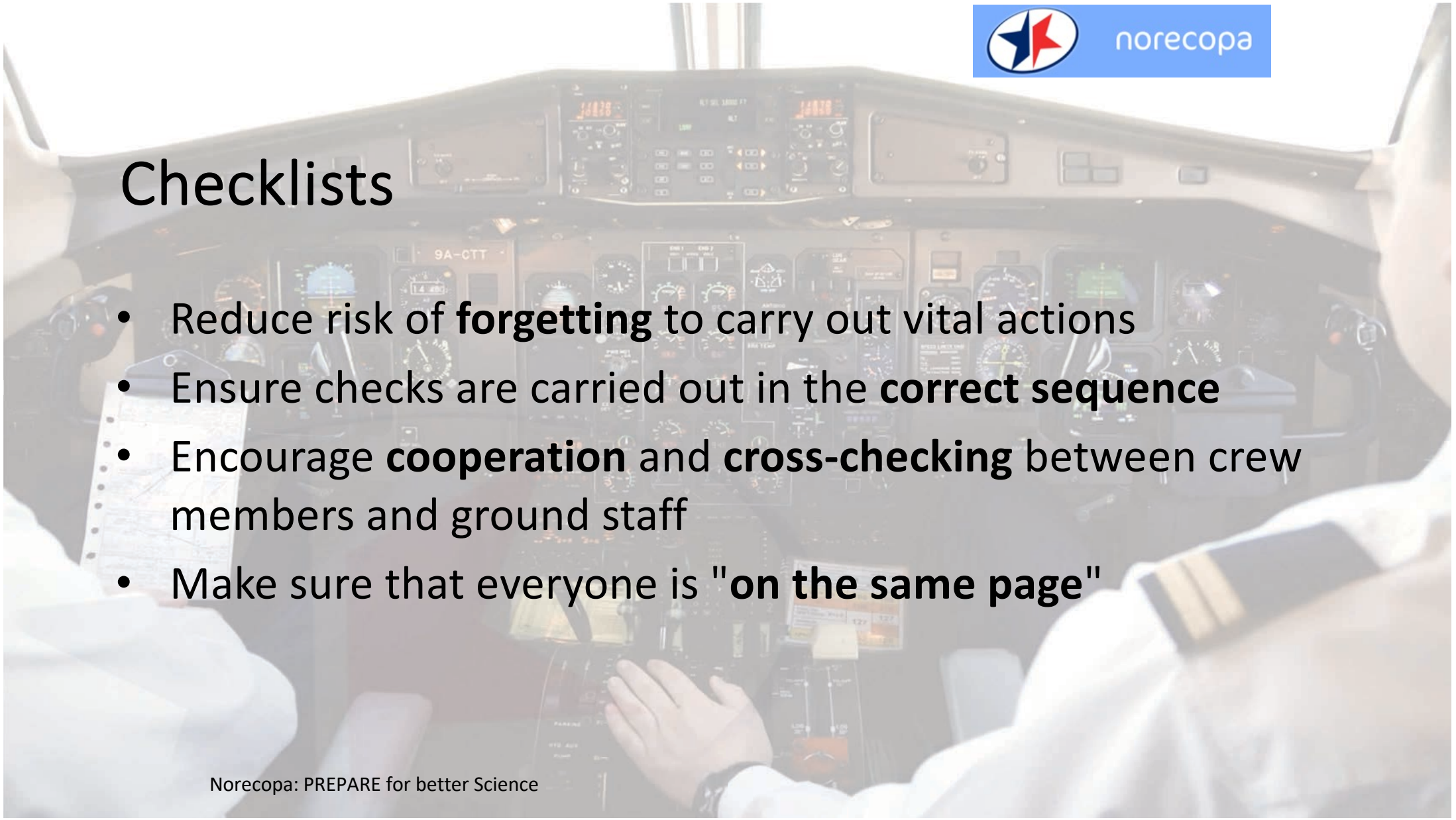
no.wikipedia.org/wiki/US_Airways_Flight_1549

en.wikipedia.org

Hudson River, 2009

All 155 passengers and crew saved

10-15 checklists even on short routine flights



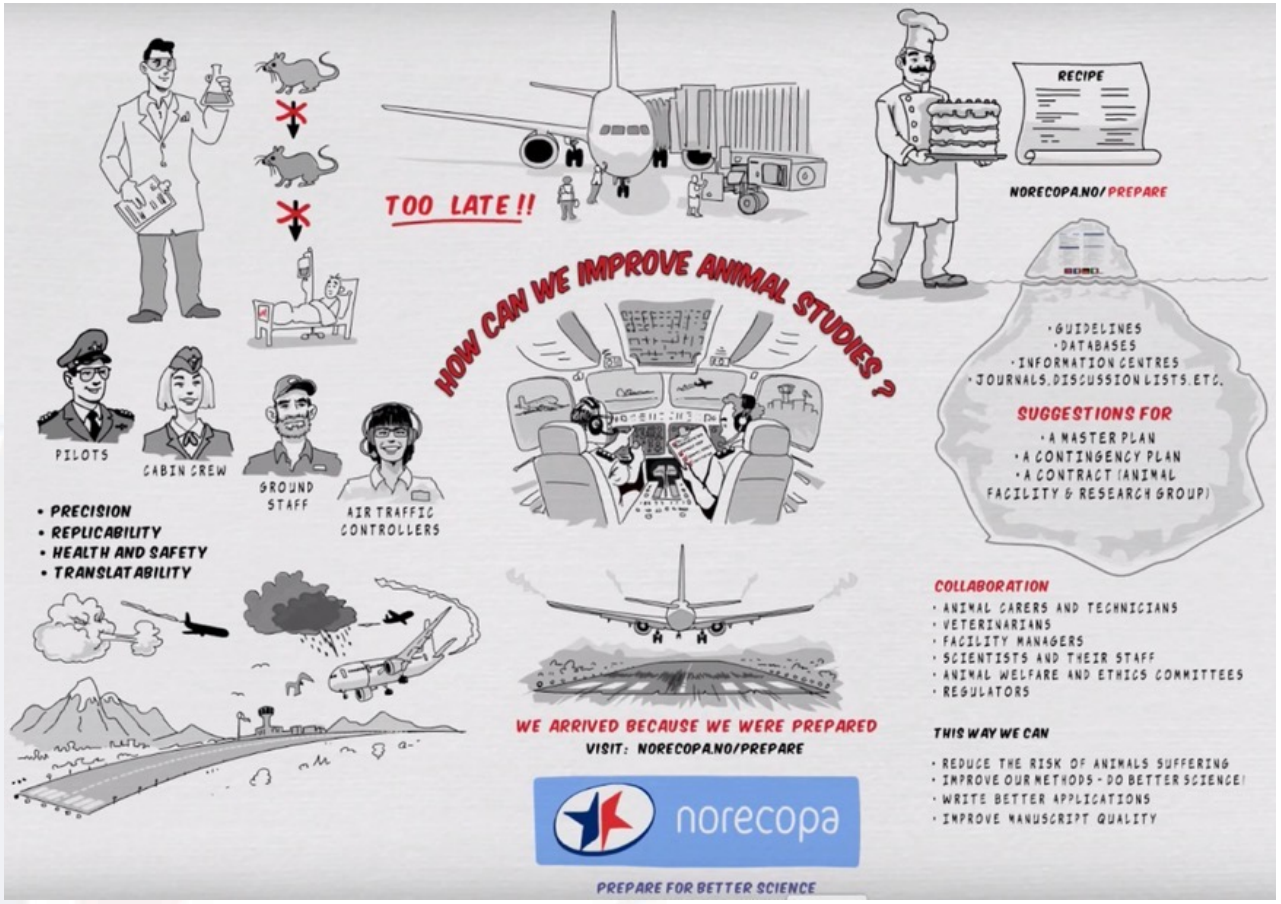
Checklists

- Reduce risk of **forgetting** to carry out vital actions
- Ensure checks are carried out in the **correct sequence**
- Encourage **cooperation** and **cross-checking** between crew members and ground staff
- Make sure that everyone is "**on the same page**"

Rapid evacuation by trained cabin crew saved many lives

norecopa.no/PREPARE/film

3-minute whiteboard film



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Surgical Safety Checklist

World Health Organization | Patient Safety
A World Alliance for Safer Health Care

Before induction of anaesthesia → **Before skin incision** → **Before patient leaves operating room**

(with at least nurse and anaesthetist) | (with nurse, anaesthetist and surgeon) | (with nurse, anaesthetist and surgeon)

Has the patient confirmed his/her identity, site, procedure, and consent?
- ☐ Yes

Is the site marked?
- ☐ Yes
- ☐ Not applicable

Is the anaesthesia machine and medication check complete?
- ☐ Yes

Is the pulse oximeter on the patient and functioning?
- ☐ Yes

Does the patient have a:

Known allergy?
- ☐ No
- ☐ Yes

Difficult airway or aspiration risk?
- ☐ No
- ☐ Yes, and equipment/assistance available

Risk of >500ml blood loss (7ml/kg in children)?
- ☐ No
- ☐ Yes, and two IVs/central access and fluids planned

☐ Confirm all team members have introduced themselves by name and role.

☐ Confirm the patient's name, procedure, and where the incision will be made.

Has antibiotic prophylaxis been given within the last 60 minutes?
- ☐ Yes
- ☐ Not applicable

Anticipated Critical Events

To Surgeon:
- ☐ What are the critical or non-routine steps?
- ☐ How long will the case take?
- ☐ What is the anticipated blood loss?

To Anaesthetist:
- ☐ Are there any patient-specific concerns?

To Nursing Team:
- ☐ Has sterility (including indicator results) been confirmed?
- ☐ Are there equipment issues or any concerns?

Is essential imaging displayed?
- ☐ Yes
- ☐ Not applicable

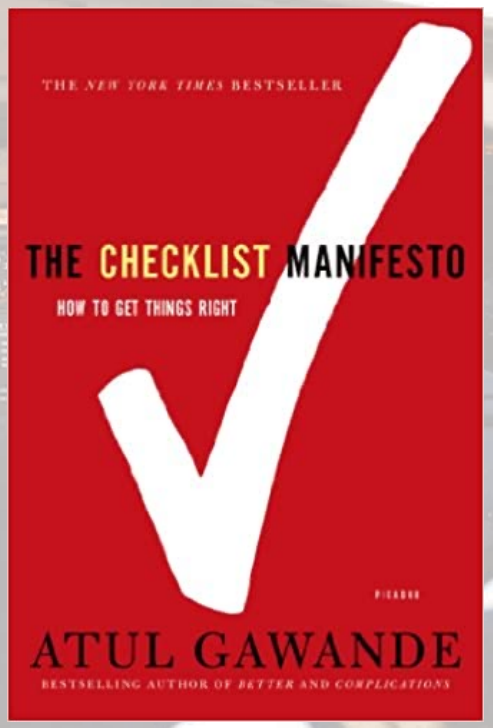
Nurse Verbally Confirms:
- ☐ The name of the procedure
- ☐ Completion of instrument, sponge and needle counts
- ☐ Specimen labelling (read specimen labels aloud, including patient name)
- ☐ Whether there are any equipment problems to be addressed

To Surgeon, Anaesthetist and Nurse:
- ☐ What are the key concerns for recovery and management of this patient?

This checklist is not intended to be comprehensive. Additions and modifications to fit local practice are encouraged.

Revised 1 / 2009

who.int/patientsafety/topics/safe-surgery/checklist/en



amazon.com/gp/product/0312430000

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PREPARE encourages scientists to collaborate with animal carers and technicians from Day 1

- they have a right to know and will be more motivated
- 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
- lack of involvement creates anxiety, depression and opposition to animal research, as well as limiting creativity which might improve the experiments

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Imagine a project:

The effect of light on the growth of forest flowers

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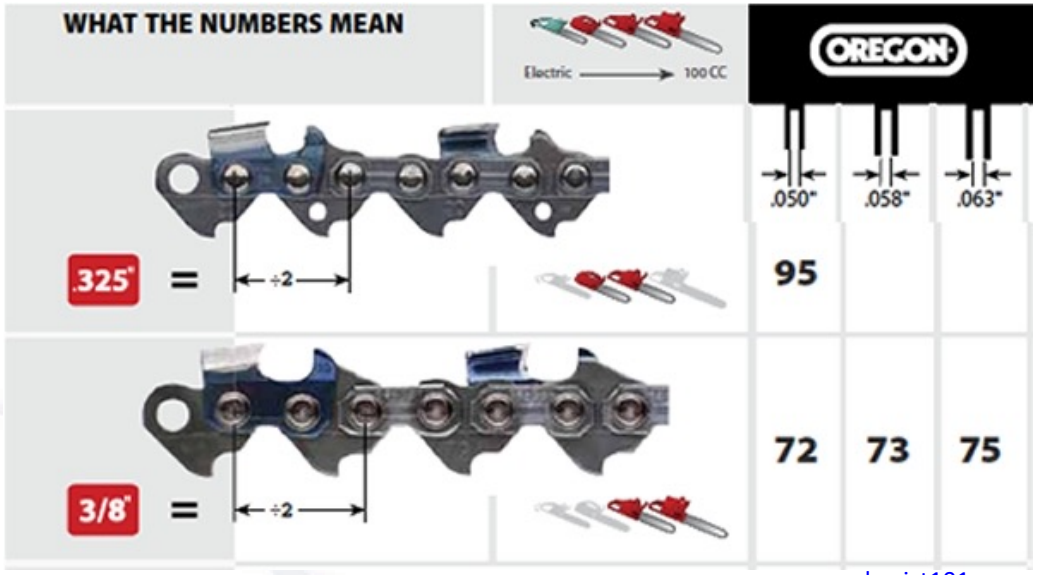
The easy parts of design and reporting:



arborist101.com

- Chainsaw
  - Blade characteristics
  - Sparkplug type
  - Petrol/oil mixture
  - Service history
- Angle of cut in tree
- Length of tree logs

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Critical issues behind the scenes that may not get reported:

- Experience of the workers
- Inspection for signs of rot and to decide felling direction
- Additional equipment (winch, chains, straps, wedges)
- Routines and equipment for sharpening the chain
- Clearing-up and transport of logs
- Health and safety precautions – clothing, onlookers
- Division of labour and costs

Starts long before the actual work.

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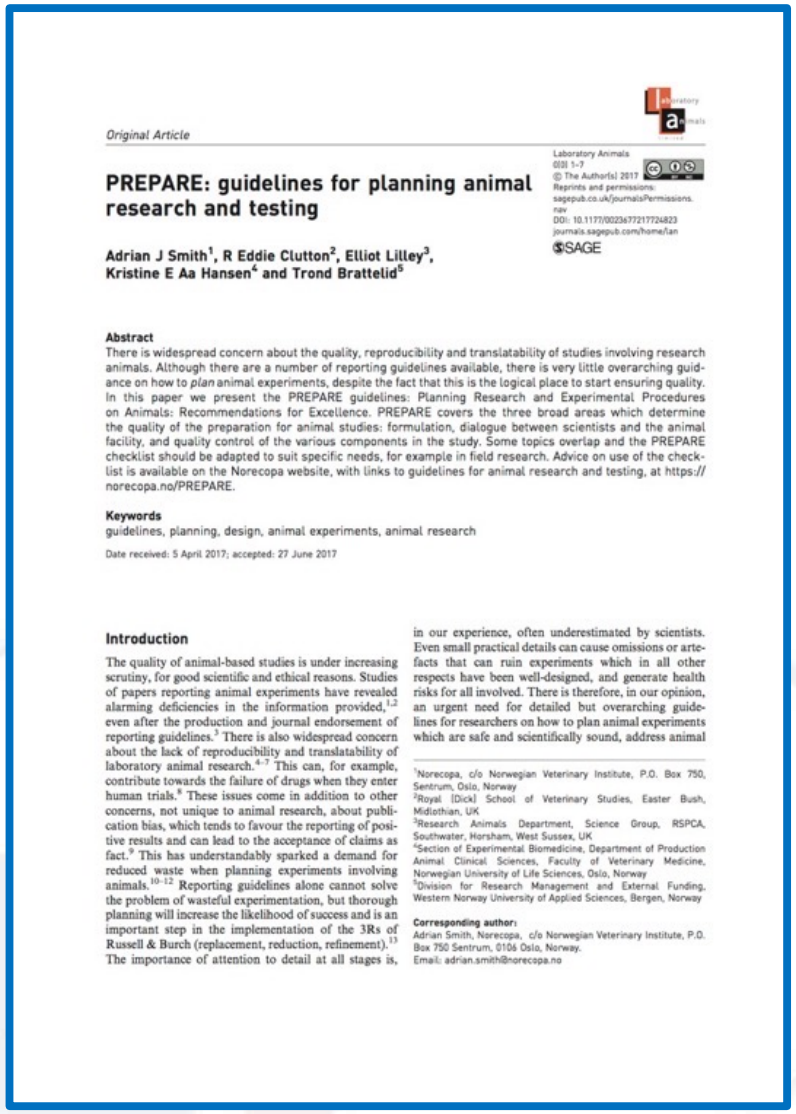
Clearing up afterwards...



Original Article

PREPARE: guidelines for planning animal research and testing

Adrian J Smith[1], R Eddie Clutton[2], Elliot Lilley[3], Kristine E Aa Hansen[4] and Trond Brattelid[5]

Laboratory Animals
0(0) 1–7

DOI: 10.1177/0023677217724823
journals.sagepub.com/home/lan
SAGE

Abstract

There is widespread concern about the quality, reproducibility and translatability of studies involving research animals. Although there are a number of reporting guidelines available, there is very little overarching guidance on how to *plan* animal experiments, despite the fact that this is the logical place to start ensuring quality. In this paper we present the PREPARE guidelines: Planning Research and Experimental Procedures on Animals: Recommendations for Excellence. PREPARE covers the three broad areas which determine the quality of the preparation for animal studies: formulation, dialogue between scientists and the animal facility, and quality control of the various components in the study. Some topics overlap and the PREPARE checklist should be adapted to suit specific needs, for example in field research. Advice on use of the checklist is available on the Norecopa website, with links to guidelines for animal research and testing, at https://norecopa.no/PREPARE.

Keywords

guidelines, planning, design, animal experiments, animal research

Date received: 5 April 2017; accepted: 27 June 2017

Introduction

The quality of animal-based studies is under increasing scrutiny, for good scientific and ethical reasons. Studies of papers reporting animal experiments have revealed alarming deficiencies in the information provided,[1,2] even after the production and journal endorsement of reporting guidelines.[3] There is also widespread concern about the lack of reproducibility and translatability of laboratory animal research.[4–7] This can, for example, contribute towards the failure of drugs when they enter human trials.[8] These issues come in addition to other concerns, not unique to animal research, about publication bias, which tends to favour the reporting of positive results and can lead to the acceptance of claims as fact.[9] This has understandably sparked a demand for reduced waste when planning experiments involving animals.[10–12] Reporting guidelines alone cannot solve the problem of wasteful experimentation, but thorough planning will increase the likelihood of success and is an important step in the implementation of the 3Rs of Russell & Burch (replacement, reduction, refinement).[13] The importance of attention to detail at all stages is, in our experience, often underestimated by scientists. Even small practical details can cause omissions or artefacts that can ruin experiments which in all other respects have been well-designed, and generate health risks for all involved. There is therefore, in our opinion, an urgent need for detailed but overarching guidelines for researchers on how to plan animal experiments which are safe and scientifically sound, address animal

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[3]Research Animals Department, Science Group, RSPCA, Southwater, Horsham, West Sussex, UK
[4]Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, Oslo, Norway
[5]Division for Research Management and External Funding, Western Norway University of Applied Sciences, Bergen, Norway

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Pre-published under Open Access on 3 August 2017, sponsored by the Universities Federation for Animal Welfare (UFAW), UK

https://doi.org/10.1177/0023677217724823

Over 34,000 views/downloads from the journal website so far

Also downloadable from norecopa.no/PREPARE

PREPARE:

Planning **R**esearch and **E**xperimental **P**rocedures on **A**nimals: **R**ecommendations for **E**xcellence

PREPARE covers 15 topics:

Formulation of the study

1. Literature searches
2. Legal issues
3. Ethical issues, harm-benefit assessment and humane endpoints
4. Experimental design and statistical analysis

Dialogue between scientists and the animal facility

5. Objectives and timescale, funding and division of labour
6. Facility evaluation
7. Education and training
8. Health risks, waste disposal and decontamination

Methods

9. Test substances and procedures
10. Experimental animals
11. Quarantine and health monitoring
12. Housing and husbandry
13. Experimental procedures
14. Humane killing, release, reuse or rehoming
15. Necropsy

Items in pink are not typically highlighted in reporting guidelines

norecopa.no/PREPARE/prepare-checklist

PREPARE

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The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

Adrian J. Smith[a], R. Eddie Clutton[b], Elliot Lilley[c], Kristine E. Aa. Hansen[d] & Trond Brattelid[e]

[a]Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; [b]Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; [c]Research Animals Department, Science Group, RSPCA, Wilberforce Way, Southwater, Horsham, West Sussex, RH13 9RS, U.K.; [d]Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, P.O. Box 8146 Dep., 0033 Oslo, Norway; [e]Division for Research Management, Sciences, 5020 Bergen, Norway.

PREPARE[1] består av retningslinjer for planlegging av dyreforsøk. Disse som f.eks. ARRIVE[2]. PREPARE dekker de tre store områdene som beste

1. **Designet av studiet**
2. **Dialogen mellom forskerne og dyreavdelingen**
3. **Kvalitetskontroll av de ulike komponentene i studiet**

I praksis vil ikke temaene alltid behandles i den rekkefølgen som er pr PREPARE-sjekklisten kan endres for å ivareta spesielle behov, f.eks. ve dyreavdelinger, fordi laboratorieforsøk er helt avhengige av deres kvalif Norecopas nettsider, med lenker til globale ressurser, på **https://norec** PREPARE-retningslinjene er et dynamisk sett som vil videreutvikles ette produseres, og etterhvert som "best praksis" innenfor forsøksdyrmiljøet forbedres.

Tema	Anbefaling
(A) Designet av studiet	
1. Litteratursøk	☐ Formulere en klar hypotese, med primære og sekundære mål. ☐ Vurdere å foreta en systematisk undersøkelse av litteraturen (Systematic Review). ☐ Bestemme hvilke databaser og informasjonsspesialister som skal brukes, og konstruere søkebegrep. ☐ Vurdere relevansen av dyrearten som skal brukes, dens biologi og egnethet til å svare på de eksperimentelle spørsmålene med minst mulig lidelse, og artens velferdsbehov. ☐ Evaluere prosjektets reproduserbarhet og overførbarhet.
2. Juridiske spørsmål	☐ Vurdere hvordan forsøket er påvirket av relevant lovgivning for dyreforsøk og andre aktuelle områder som f.eks. dyretransport og helse, miljø og sikkerhet. ☐ Finne relevante veiledningsdokumenter (f.eks. EUs retningslinjer for prosjektevaluering).
3. Etiske spørsmål, kostnad-nytteanalyse og humane endepunkter	☐ Skrive et sammendrag av prosjektet på legmannsspråk. ☐ I dialog med etiske komitéer, vurdere om uttalelser om denne typen forsøk er allerede blitt produsert. ☐ Adressere "de 3 R-ene" (Replacement, Reduction, Refinement) og "de 3 S-ene" (Good Science, Good Sense, Good Sensibilities). ☐ Vurdere forhåndsregistrering av forsøket og publisering av negative resultater. ☐ Foreta en kostnad-nytteanalyse ("Harm-Benefit Assessment") og diskutere eventuelle lidelser som kan oppstå under forsøket. ☐ Diskutere læringsmålene dersom dyrene skal brukes i undervisnings- eller treningsøyemed. ☐ Klassifisere prosjektet etter belastningsgraden. ☐ Definere objektive, lett målbare og utvetydige humane endepunkter. ☐ Diskutere behovet (hvis det er noe) for å bruke død som endepunktet for forsøket.
4. Eksperimentelt design og statistisk analyse	☐ Vurdere pilotforsøk og diskutere statistisk styrke og signifikansnivåer. ☐ Definere den eksperimentelle enheten og bestemme antallet forsøksdyr. ☐ Bestemme metodene for randomisering, forhindre observasjonsskjevheter, og bestemme inklusjons- og eksklusjonskriterier.

+ 2 online versions
35 languages

Tema	Anbefaling
(B) Dialogen mellom forskerne og dyreavdelingen	
5. Mål og tidshorisont, finansiering og arbeidsfordeling	☐ Arrangere møter med alle relevante personell når tidlige planer for prosjektet foreligger. ☐ Lag en omtrentlig tidsramme for prosjektet, som viser behovene for assistanse med forberedelser, dyrestell, prosedyrer og avfallshåndtering/dekontaminasjon. ☐ Diskutere og legge frem alle forventede og potensielle kostnader. ☐ Lage en detaljert plan for fordelingen av både arbeidsoppgavene og utgiftene, på alle stadiene i forsøket.
	fasilitetene, for å evaluere bygningsmassen, standarden på utstyret og
	ved perioder med ekstra risiko.
	rtansen hos personalet og evaluere behovet for videreutdanning og
	en, foreta en risikoevaluering som omfatter alle personene og dyrene direkte, av studiet. dusere, spesifikke retningslinjer for alle stadiene av prosjektet. , dekontaminere og avhende alt utstyret som skal brukes i studiet.
(C) Kvalitetskontroll av de ulike komponentene i studiet	
9. Testsubstanser og -prosedyrer	☐ Oppgi så mye informasjon som mulig om testsubstansene. ☐ Evaluere gjennomførbarheten og validiteten av testprosedyrene, og de praktiske ferdighetene som er nødvendige for å gjennomføre dem.
10. Forsøksdyr	☐ Bestemme egenskapene til dyrene som er essensielle for studiet og som må rapporteres. ☐ Unngå produksjon av overskuddsdyr.
11. Karantene og helsemonitorering	☐ Diskutere dyrenes sannsynlige helsestatus, og eventuelle behov for transport, karantene og isolasjon, samt helsemonitorering og konsekvensene for personalet.
12. Oppstalling og stell	☐ Ta hensyn til dyrenes spesifikke instinkter og behov, i samråd med eksperter. ☐ Diskutere akklimatisering, optimale oppstallingsforhold og prosedyrer, miljøfaktorer og eventuelle begrensninger på disse (f.eks. fasting eller oppstalling i enebur).
13. Eksperimentelle prosedyrer	☐ Utvikle optimale metoder for fangst, immobilisering, merking og frisetting eller omplassering. ☐ Utvikle optimale metoder for å gi dyrene behandling, samt for prøvetaking, sedasjon og anestesi, kirurgi og andre inngrep.
14. Human avliving, frisettelse eller omplassering	☐ Konsultere relevant lovgivning og retningslinjer i god tid før studiet. ☐ Definere de primære metodene for avliving, samt metoder som kan brukes i en nødssituasjon. ☐ Evaluere kompetansen til personene som må foreta disse handlingene.
15. Obduksjon	☐ Lage en systematisk plan for alle stadiene i obduksjonen, inkl. hvor den skal foregå, og identifikasjon av alle dyrene og prøvene som tas.

Referanser

1. Smith AJ, Clutton RE, Lilley E, Hansen KEA & Brattelid T. PREPARE:Guidelines for Planning Animal Research and Testing. *Laboratory Animals*, 2017, DOI: 10.1177/0023677217724823.
2. Kilkenny C, Browne WJ, Cuthill IC *et al.* Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. *PloS Biology*, 2010; DOI: 10.1371/journal.pbio.1000412.

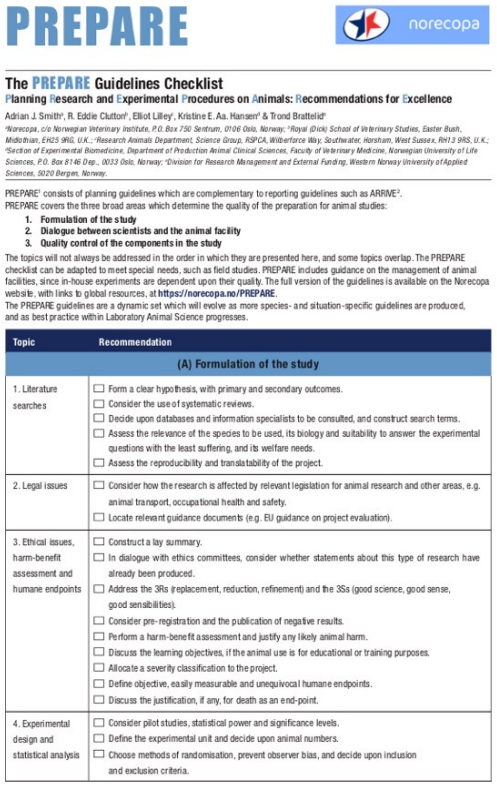
Mer informasjon
https://norecopa.no/PREPARE / *post@norecopa.no* / @norecopa

Norecopa: PREPARE for better Science

norecopa.no/PREPARE/prepare-checklist

Three versions of the checklist:

1. plain pdf file



PREPARE norecopa

The PREPARE Guidelines Checklist
Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

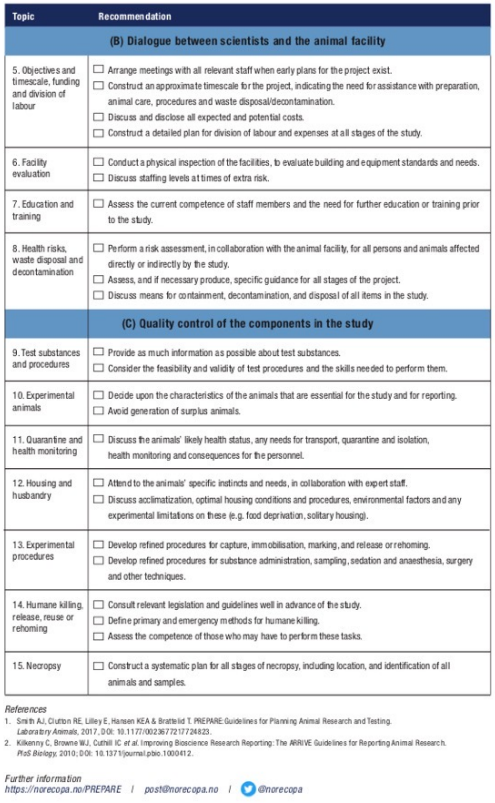
Adrian J. Smith[a], R. Eddie Clutton[b], Elliot Lilley[c], Kristine E. Aa. Hansen[d] & Trond Brattelid[e]
[a]Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; [b]Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; [c]Research Animals Department, Science Group, RSPCA, Wilberforce Way, Southwater, Horsham, West Sussex, RH13 9RS, U.K.; [d]Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, P.O. Box 8146 Dep., 0033 Oslo, Norway; [e]Division for Research Management and External Funding, Western Norway University of Applied Sciences, 5020 Bergen, Norway.

PREPARE[1] consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE[2].
PREPARE covers the three broad areas which determine the quality of the preparation for animal studies:

1. **Formulation of the study**
2. **Dialogue between scientists and the animal facility**
3. **Quality control of the components in the study**

The topics will not always be addressed in the order in which they are presented here, and some topics overlap. The PREPARE checklist can be adapted to meet special needs, such as field studies. PREPARE includes guidance on the management of animal facilities, since in-house experiments are dependent upon their quality. The full version of the guidelines is available on the Norecopa website, with links to global resources, at **https://norecopa.no/PREPARE**.
The PREPARE guidelines are a dynamic set which will evolve as more species- and situation-specific guidelines are produced, and as best practice within Laboratory Animal Science progresses.

Topic	Recommendation
(A) Formulation of the study	
1. Literature searches	☐ Form a clear hypothesis, with primary and secondary outcomes. ☐ Consider the use of systematic reviews. ☐ Decide upon databases and information specialists to be consulted, and construct search terms. ☐ Assess the relevance of the species to be used, its biology and suitability to answer the experimental questions with the least suffering, and its welfare needs. ☐ Assess the reproducibility and translatability of the project.
2. Legal issues	☐ Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety. ☐ Locate relevant guidance documents (e.g. EU guidance on project evaluation).
3. Ethical issues, harm-benefit assessment and humane endpoints	☐ Construct a lay summary. ☐ In dialogue with ethics committees, consider whether statements about this type of research have already been produced. ☐ Address the 3Rs (replacement, reduction, refinement) and the 3Ss (good science, good sense, good sensibilities). ☐ Consider pre-registration and the publication of negative results. ☐ Perform a harm-benefit assessment and justify any likely animal harm. ☐ Discuss the learning objectives, if the animal use is for educational or training purposes. ☐ Allocate a severity classification to the project. ☐ Define objective, easily measurable and unequivocal humane endpoints. ☐ Discuss the justification, if any, for death as an end-point.
4. Experimental design and statistical analysis	☐ Consider pilot studies, statistical power and significance levels. ☐ Define the experimental unit and decide upon animal numbers. ☐ Choose methods of randomisation, prevent observer bias, and decide upon inclusion and exclusion criteria.



Topic	Recommendation
(B) Dialogue between scientists and the animal facility	
5. Objectives and timescale, funding and division of labour	☐ Arrange meetings with all relevant staff when early plans for the project exist. ☐ Construct an approximate timescale for the project, indicating the need for assistance with preparation, animal care, procedures and waste disposal/decontamination. ☐ Discuss and disclose all expected and potential costs. ☐ Construct a detailed plan for division of labour and expenses at all stages of the study.
6. Facility evaluation	☐ Conduct a physical inspection of the facilities, to evaluate building and equipment standards and needs. ☐ Discuss staffing levels at times of extra risk.
7. Education and training	☐ Assess the current competence of staff members and the need for further education or training prior to the study.
8. Health risks, waste disposal and decontamination	☐ Perform a risk assessment, in collaboration with the animal facility, for all persons and animals affected directly or indirectly by the study. ☐ Assess, and if necessary produce, specific guidance for all stages of the project. ☐ Discuss means for containment, decontamination, and disposal of all items in the study.
(C) Quality control of the components in the study	
9. Test substances and procedures	☐ Provide as much information as possible about test substances. ☐ Consider the feasibility and validity of test procedures and the skills needed to perform them.
10. Experimental animals	☐ Decide upon the characteristics of the animals that are essential for the study and for reporting. ☐ Avoid generation of surplus animals.
11. Quarantine and health monitoring	☐ Discuss the animals' likely health status, any needs for transport, quarantine and isolation, health monitoring and consequences for the personnel.
12. Housing and husbandry	☐ Attend to the animals' specific instincts and needs, in collaboration with expert staff. ☐ Discuss acclimatization, optimal housing conditions and procedures, environmental factors and any experimental limitations on these (e.g. food deprivation, solitary housing).
13. Experimental procedures	☐ Develop refined procedures for capture, immobilisation, marking, and release or rehoming. ☐ Develop refined procedures for substance administration, sampling, sedation and anaesthesia, surgery and other techniques.
14. Humane killing, release, reuse or rehoming	☐ Consult relevant legislation and guidelines well in advance of the study. ☐ Define primary and emergency methods for humane killing. ☐ Assess the competence of those who may have to perform these tasks.
15. Necropsy	☐ Construct a systematic plan for all stages of necropsy, including location, and identification of all animals and samples.

References
1. Smith AJ, Clutton RE, Lilley E, Hansen KEA & Brattelid T. PREPARE: Guidelines for Planning Animal Research and Testing. *Laboratory Animals*, 2017, DOI: 10.1177/0023677217724823.
2. Kilkenny C, Browne WJ, Cuthill IC *et al.* Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. *PLoS Biology*, 2010; DOI: 10.1371/journal.pbio.1000412.

Further information
https://norecopa.no/PREPARE | *post@norecopa.no* | *@norecopa*

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2. fillable pdf file

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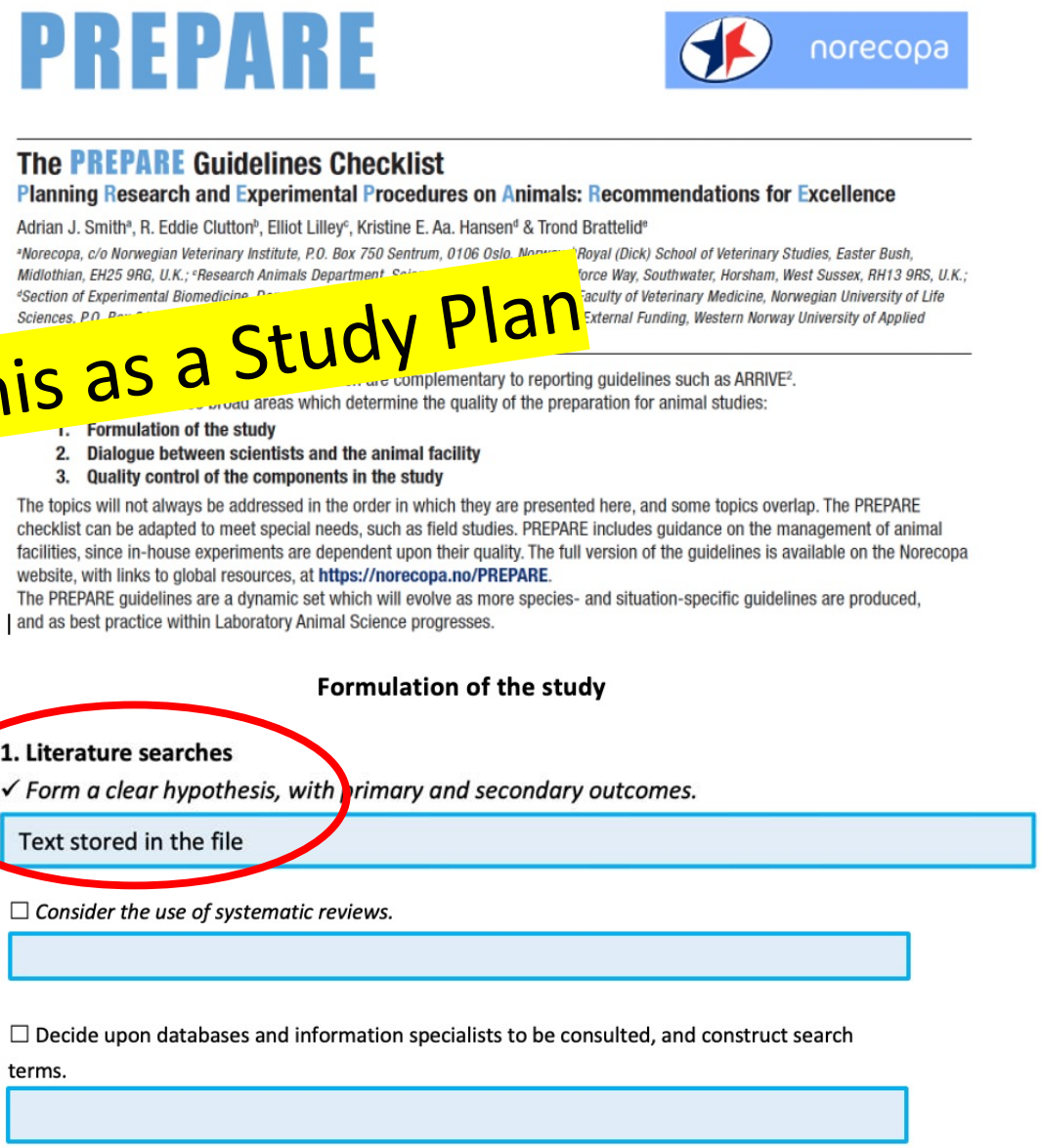

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You can use this as a Study Plan

are complementary to reporting guidelines such as ARRIVE[2].

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Formulation of the study

1. Literature searches

✓ *Form a clear hypothesis, with primary and secondary outcomes.*

Text stored in the file

☐ *Consider the use of systematic reviews.*

☐ Decide upon databases and information specialists to be consulted, and construct search terms.

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Three versions of the checklist:

3. online version

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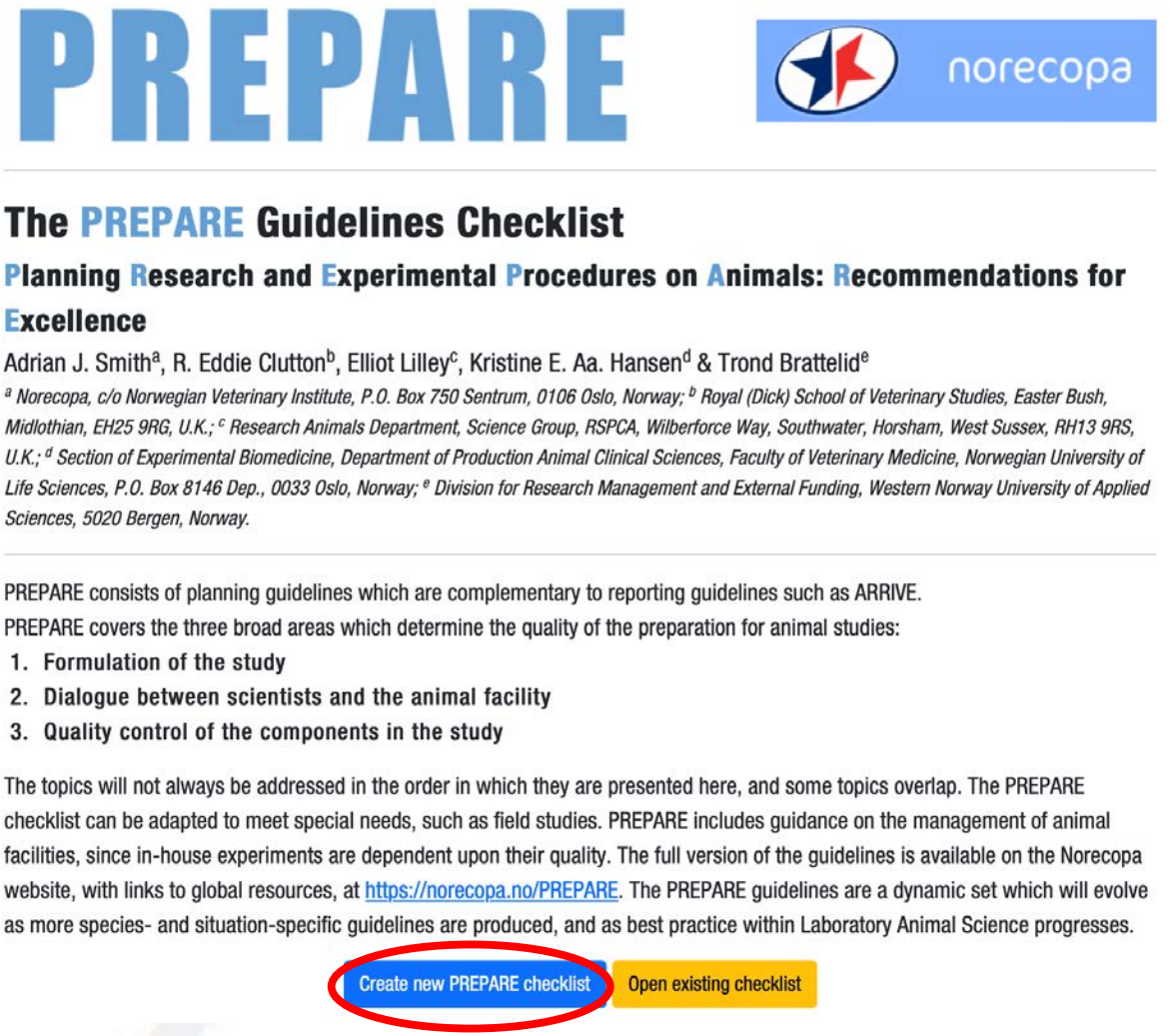

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Create new PREPARE checklist Open existing checklist

Your auth code for this checklist is **deeb7d** Please save this code so you are able to open your checklist at a later time. You can also bookmark this page.

Topic	Recommendation
(A) Formulation of the study	
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2. Legal issues	Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety.

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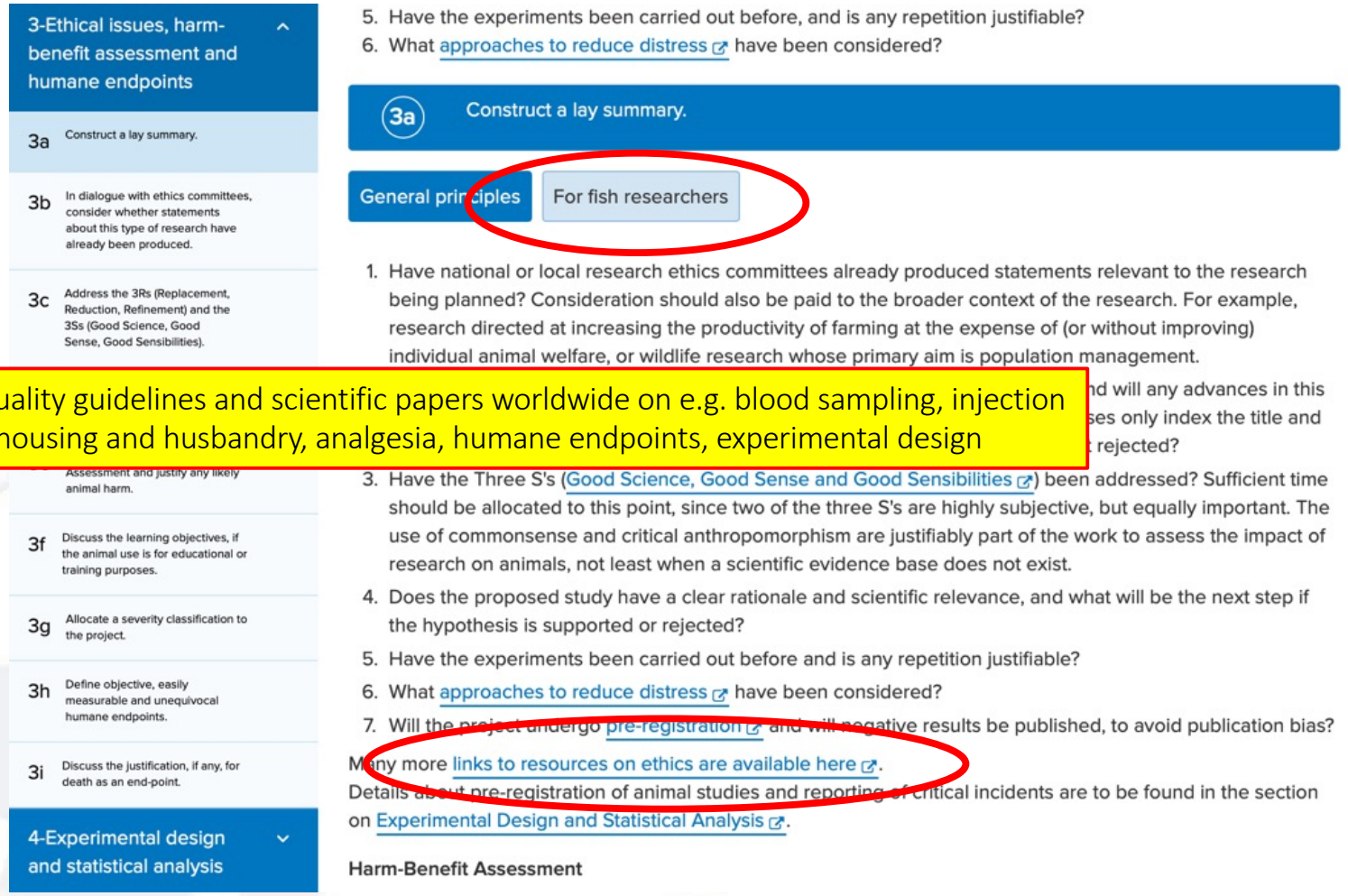

Links to quality guidelines and scientific papers worldwide on e.g. blood sampling, injection volumes, housing and husbandry, analgesia, humane endpoints, experimental design

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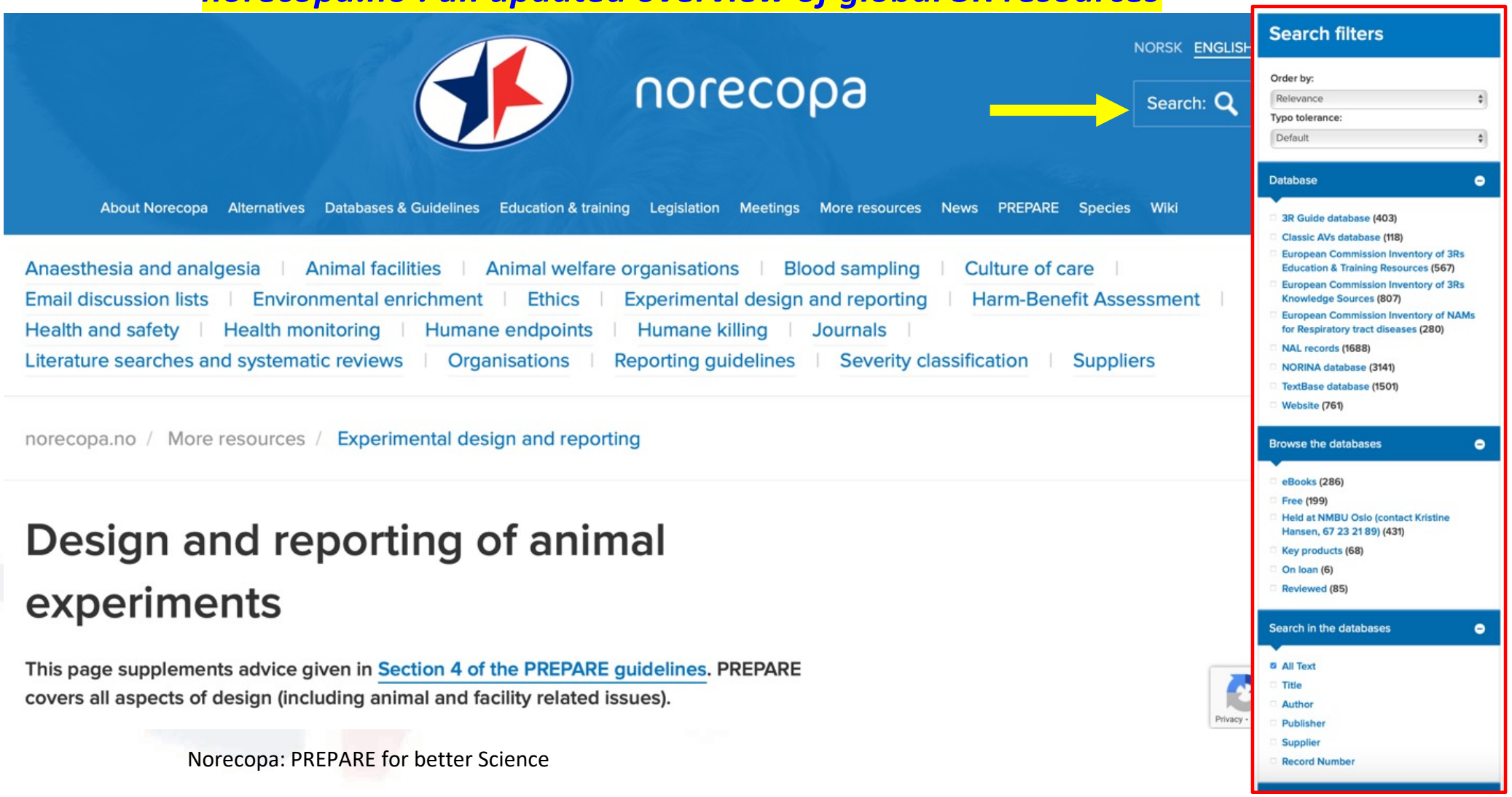
PREPARE is closely linked to

norecopa.no : an updated overview of global 3R resources



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3R-resources can be 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 3R terms
- We have no single ”Journal of 3R-resources”

The EURL ECVAM **Search** Guide

Can be ordered free of charge from

bookshop.europa.eu

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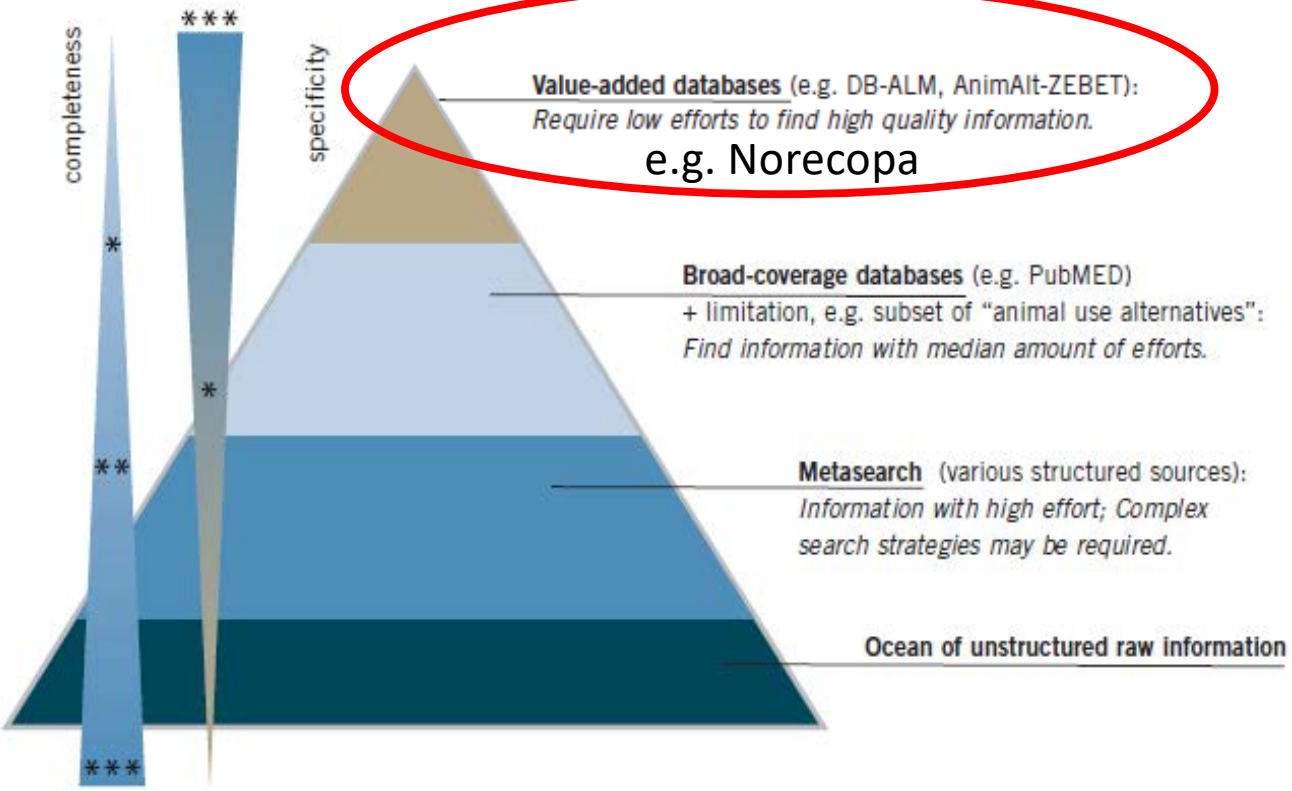
completeness
specificity
***
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***
Value-added databases (e.g. DB-ALM, AnimAlt-ZEBET):
Require low efforts to find high quality information.
e.g. Norecopa
Broad-coverage databases (e.g. PubMED)
+ limitation, e.g. subset of "animal use alternatives":
Find information with median amount of efforts.
Metasearch (various structured sources):
Information with high effort; Complex search strategies may be required.
Ocean of unstructured raw information


GOOD SEARCH PRACTICE
on Animal Alternatives

Databases & Guidelines

Published lists of resources are difficult to search and quickly become outdated. Lists on a website are easier to search, but do not enable the use of filters or intelligent search engines.
Norecopa has therefore constructed four databases, which together with all the text on this website can be searched simultaneously using the search field at the top of every page.

- 3R Guide: a global overview of **databases, guidelines, information centres, journals, email lists, regulations and policies** which may be of use when planning experiments which might include animals. A quick overview of all the guidelines can be accessed here. Norecopa has written several of these, including the PREPARE guidelines for planning animal research and testing.
- NORINA: a global overview of audiovisual aids and other items which may be used as **alternatives or supplements to animals in education and training** at all levels from junior school to University, including dissection alternatives and surgical simulators.
- TextBase: a global overview of **textbooks and other literature within laboratory animal science** and related topics.
- Classic AVs: a subset of NORINA covering **audiovisual aids that are based on older technology**.

These databases are updated regularly. Please give us feedback if you discover errors or omissions.

The Norecopa website also includes four other collections:

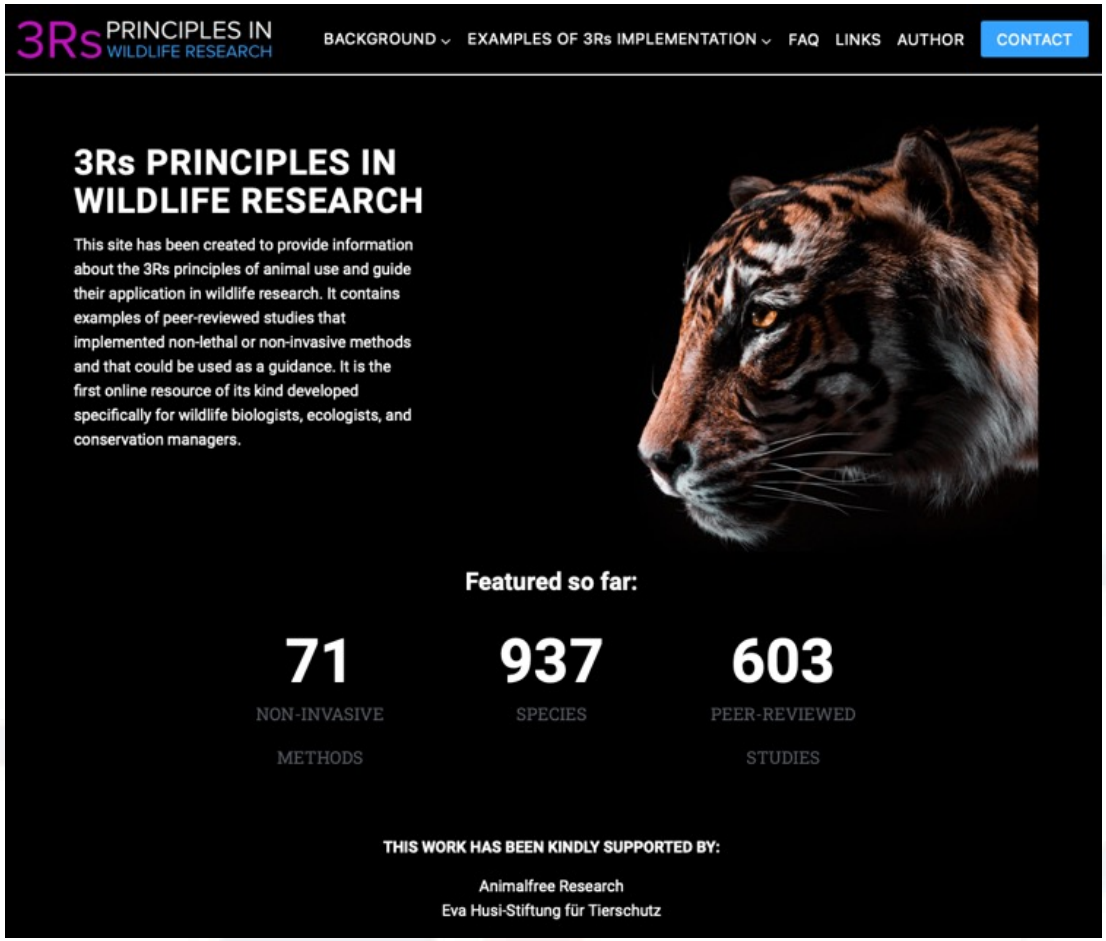
- NAL: a collection of literature references relating to the 3Rs from the US National Agricultural Library
- European Commission datasets:
  - 3Rs Knowledge Sources: over 800 resources collected by the Commission in 2016
  - 3Rs Education and Training Resources, over 560 items collected in 2018
  - Non-animal models for respiratory tract diseases, over 280 models identified in a literature review of over 21,000 publications

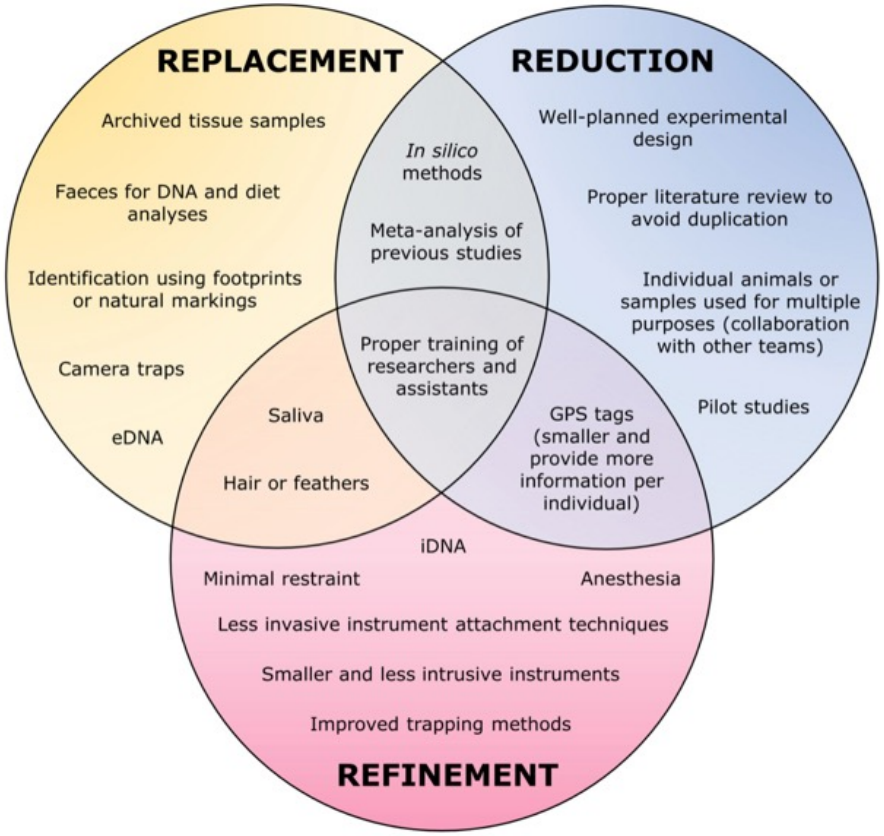
Here is an alphabetical global list of all the databases cited on the Norecopa website.

norecopa.no/databases-guidelines

links to over 70 other databases

3rswildlife.info





Source: Zemanova 2020

Miriam Zemanova

norecopa.no/**3RGuide**

Links to over 400 guidelines

A good practice guide to the administration of substances and removal of blood, including routes and volumes

3R Guide database/c6721 (legacy id: 15079)

This paper provides the researcher in the safety evaluation laboratory with an up-to-date, easy-to-use set of data sheets to aid in the study design process whilst at the same time affording maximum welfare considerations to the experimental animals.

A guide to defining and implementing protocols for the welfare assessment of laboratory animals

3R Guide database/68ba4 (legacy id: 15065)

Eleventh report of the BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement

A guide to the care and use of native Australian mammals in research and teaching

3R Guide database/502ff (legacy id: 15377)

The Guide supports implementation of the Australian Code for the care and use of animals for scientific purposes (8th edition, 2013) and ensures that the specific and unique needs of Australian native mammals are met when these animals are used for scientific purposes.

AAALAC Position Statements

3R Guide database/ef566 (legacy id: 15155)

In connection with its work of accreditation of animal care and use programmes, AAALAC International has issued position statements on a number of key elements in such a programme.

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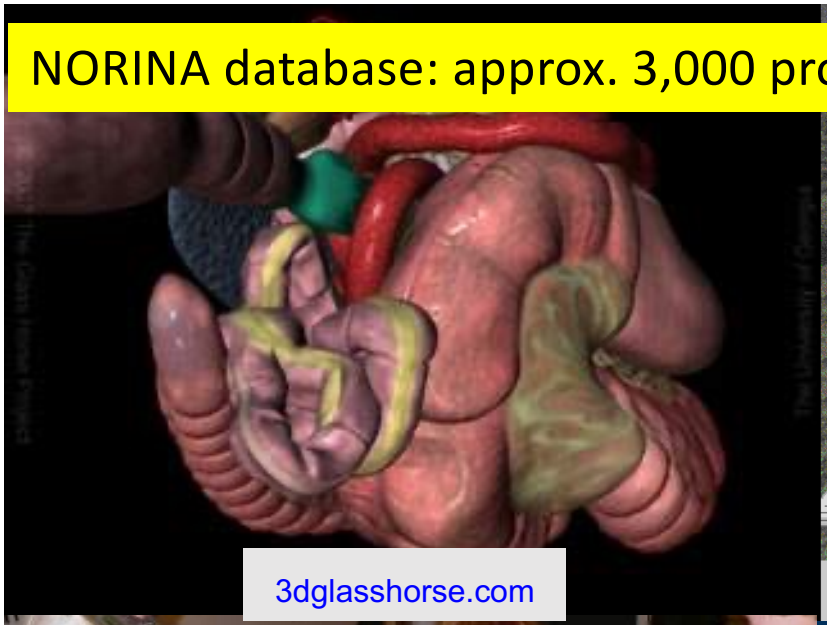
NORINA database: approx. 3,000 products



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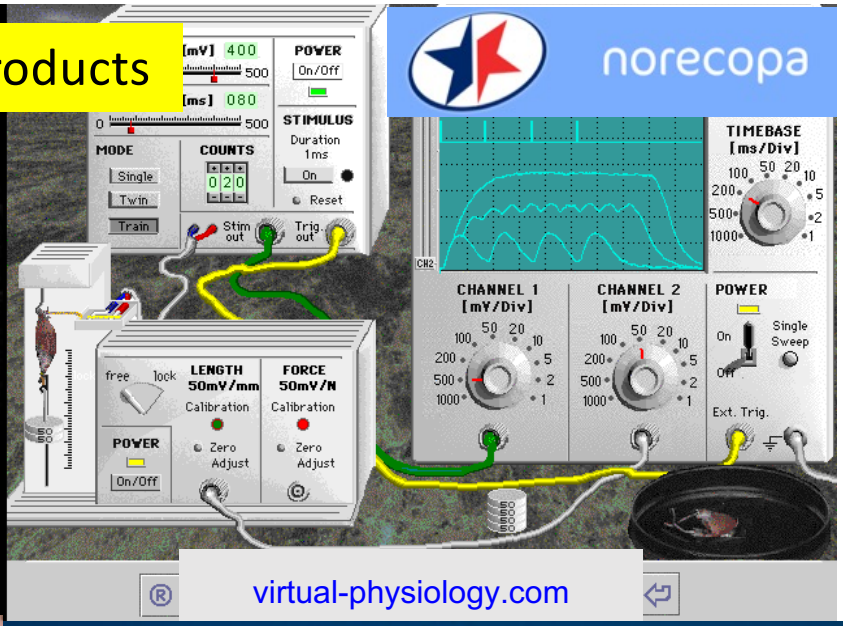

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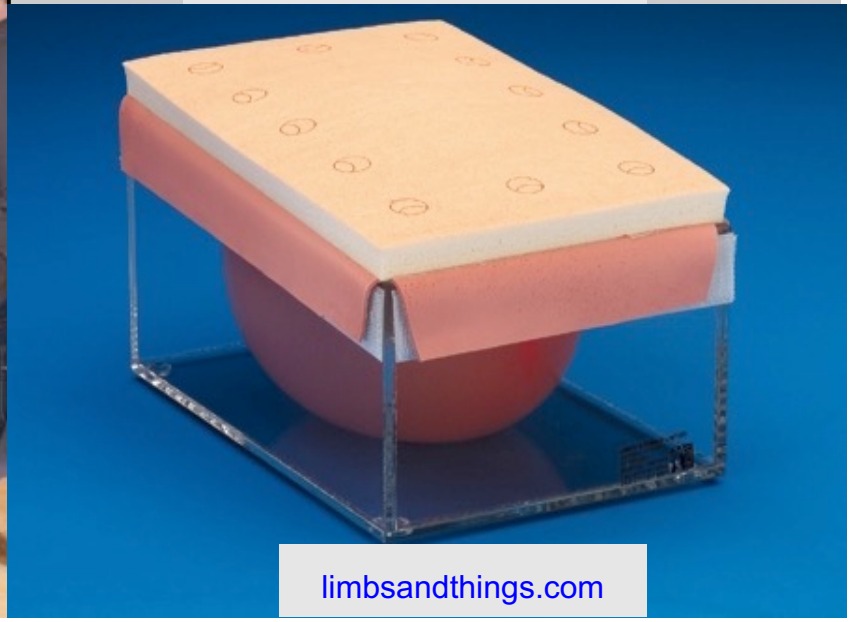
rescuecritters.com



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Rat s.c. injection
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Rat i.p. injection (method 2)
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Testing anaesthetic depth in the chicken
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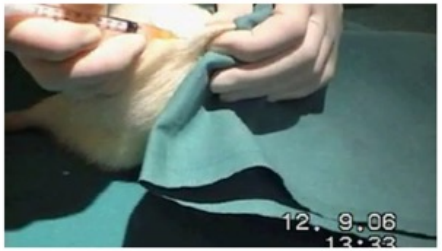
Blood collection from the saphenous vein in the mouse
Norecopa | 6,777 views



Subcutaneous injection in the rat - Technique 1
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Blood san
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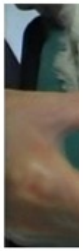
Blood san
Norecop



Blood san
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Blood sampling from the pig
Norecopa | 3,914 views

Intravenous injection in a rabbit
Norecopa | 2,025 views

Lifting a rabbit
Norecopa | 2,420 views

Subcutaneous injection in the rabbit
Norecopa | 1,479 views

Subcutaneous injection in the chicken
Norecopa | 1,806 views

Immobilisation of the rabbit
Norecopa | 2,072 views

Norecopa: PREPARE for better Science

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researchanimaltraining.com

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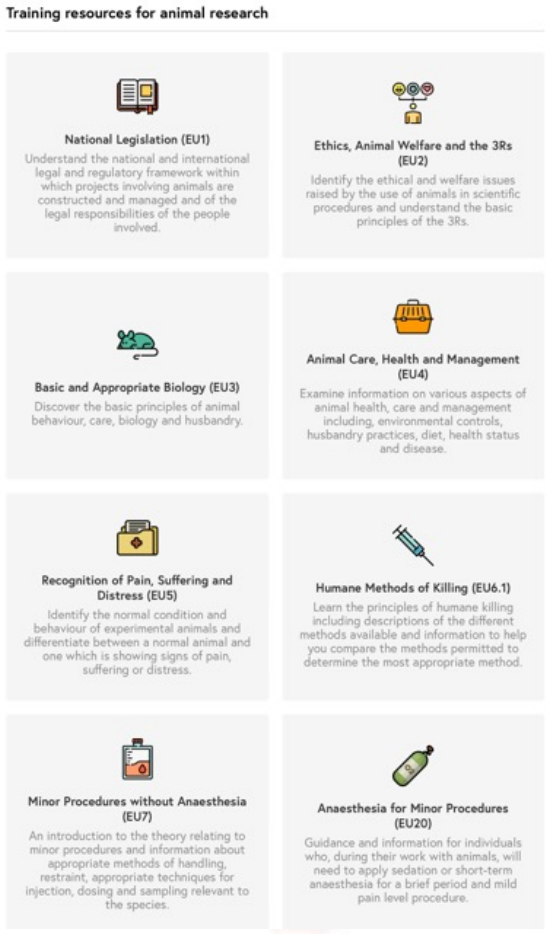
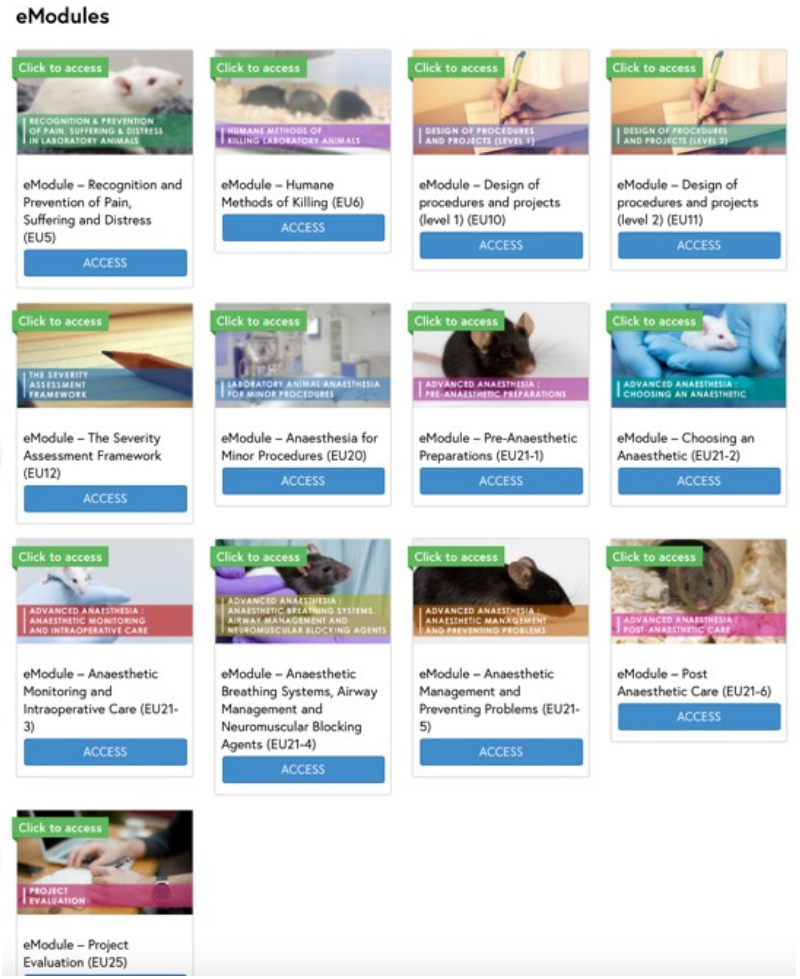




TextBase:

1,500 books related to Laboratory Animal Science:

norecopa.no/textbase

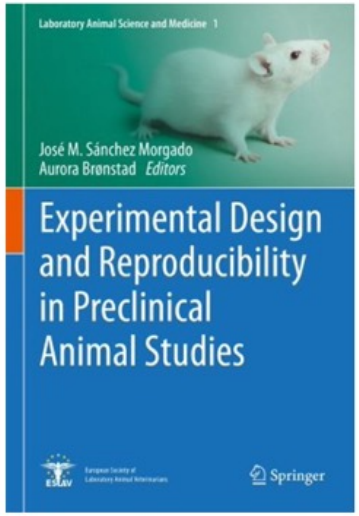
Experimental Design and Reproducibility in Preclinical Animal Studies

By José M. Sánchez Morgado & Aurora Brønstad (Eds.)

Record number: 8619d

This book provides grounds on how to plan and conduct animal experiments that can be reproduced by others. It touches on factors that may impact the reproducibility of animal studies including: the animal genetic background, the animal microbial flora, environmental and physiological variables affecting the animal, animal welfare, statistics and experimental design, systematic reviews of animal studies, and the publishing process.

The book addresses advanced undergraduates, graduate students and all scientists working with animals.



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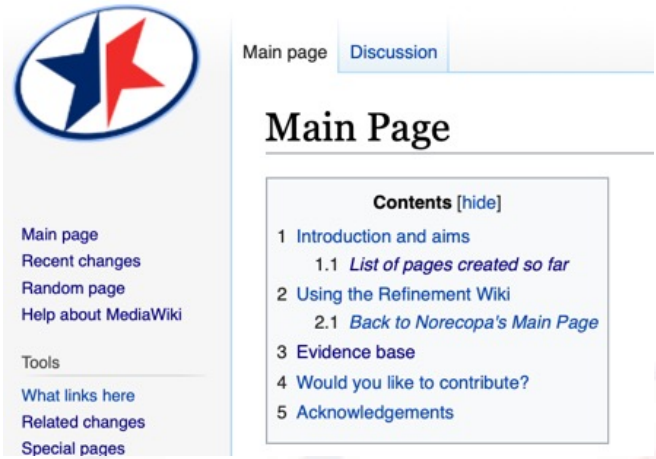
The Refinement Wiki



Susanna Louihimies

wiki.norecopa.no

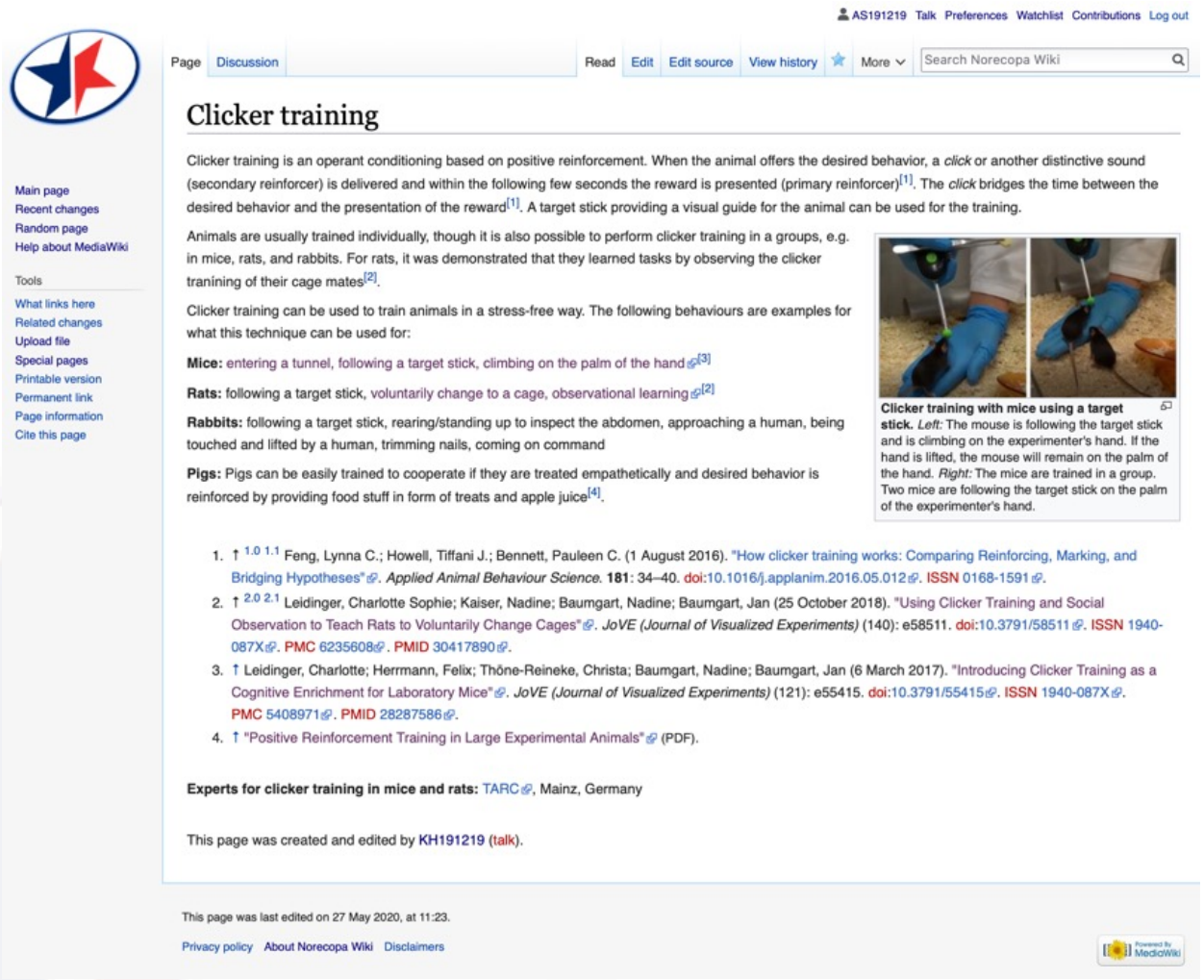
Born from the knowledge that a lot of good ideas on refinement circulate on discussion forums, but never get published.

Designed to be

- a portal for rapid publication and dissemination of these ideas
- a place to identify experts on specific refinement techniques

wiki.norecopa.no

Return to homepage



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Clicker training

Clicker training is an operant conditioning based on positive reinforcement. When the animal offers the desired behavior, a *click* or another distinctive sound (secondary reinforcer) is delivered and within the following few seconds the reward is presented (primary reinforcer)[1]. The *click* bridges the time between the desired behavior and the presentation of the reward[1]. A target stick providing a visual guide for the animal can be used for the training.

Animals are usually trained individually, though it is also possible to perform clicker training in a groups, e.g. in mice, rats, and rabbits. For rats, it was demonstrated that they learned tasks by observing the clicker tranining of their cage mates[2].

Clicker training can be used to train animals in a stress-free way. The following behaviours are examples for what this technique can be used for:

Mice: entering a tunnel, following a target stick, climbing on the palm of the hand[3]

Rats: following a target stick, voluntarily change to a cage, observational learning[2]

Rabbits: following a target stick, rearing/standing up to inspect the abdomen, approaching a human, being touched and lifted by a human, trimming nails, coming on command

Pigs: Pigs can be easily trained to cooperate if they are treated empathetically and desired behavior is reinforced by providing food stuff in form of treats and apple juice[4].

Clicker training with mice using a target stick. *Left:* The mouse is following the target stick and is climbing on the experimenter's hand. If the hand is lifted, the mouse will remain on the palm of the hand. *Right:* The mice are trained in a group. Two mice are following the target stick on the palm of the experimenter's hand.

1. ↑ 1.0 1.1 Feng, Lynna C.; Howell, Tiffani J.; Bennett, Pauleen C. (1 August 2016). "How clicker training works: Comparing Reinforcing, Marking, and Bridging Hypotheses". *Applied Animal Behaviour Science*. **181**: 34–40. doi:10.1016/j.applanim.2016.05.012. ISSN 0168-1591.
2. ↑ 2.0 2.1 Leidinger, Charlotte Sophie; Kaiser, Nadine; Baumgart, Nadine; Baumgart, Jan (25 October 2018). "Using Clicker Training and Social Observation to Teach Rats to Voluntarily Change Cages". *JoVE (Journal of Visualized Experiments)* (140): e58511. doi:10.3791/58511. ISSN 1940-087X. PMC 6235608. PMID 30417890.
3. ↑ Leidinger, Charlotte; Herrmann, Felix; Thöne-Reineke, Christa; Baumgart, Nadine; Baumgart, Jan (6 March 2017). "Introducing Clicker Training as a Cognitive Enrichment for Laboratory Mice". *JoVE (Journal of Visualized Experiments)* (121): e55415. doi:10.3791/55415. ISSN 1940-087X. PMC 5408971. PMID 28287586.
4. ↑ "Positive Reinforcement Training in Large Experimental Animals" (PDF).

Experts for clicker training in mice and rats: TARC, Mainz, Germany

This page was created and edited by KH191219 (talk).

This page was last edited on 27 May 2020, at 11:23.

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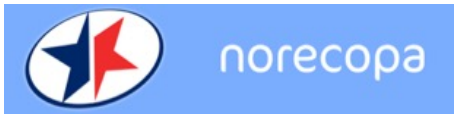


- Acclimatisation
- Adrian Smith
- Alphaxalone
- Anaesthesia in neonates
- Analgesia
- Asepsis
- Blood sampling of hamsters
- Blood sampling of pigs
- Blood sampling of rainbow trout
- Breeding strategies for mice
- Clicker training
- Contingency plans
- Decapitation
- Detecting early onset of clinical signs in the mouse model of Covid-19
- Detection of pain and distress in mice
- EMLA cream
- Embryo transfer
- Experimental Autoimmune Encephalomyeltis (EAE)
- Facial expression analysis
- Food crunchers
- General discusson on use of analgesics
- Genotyping mice
- Habituation training
- High-fat diets
- Hot Bead Sterilisers
- Housing nude mice
- Housing research fish
- Humane endpoints
- Hydrodynamic gene delivery
- Intra-ocular injections
- Intranasal administration
- Intraperitoneal injection
- Intraperitoneal pentobarbitone
- Ketamine and alpha-2 agonist combinations
- Long-term anaesthesia in rodents
- Lumpfish
- Main Page
- Marble Burying Test
- Metabolic cages
- Minipumps
- Montanide adjuvant
- Mouse Grimace Scale
- Mouse handling
- Nest building material
- Oestrus suppression in ferrets
- Pneumocystis murina
- Recapping needles
- Rotarod Test
- Screening cell lines
- Sedation of cattle
- Splenectomy
- Sterilisation of instruments
- TTEAM and TTouch
- Tail vein injection
- Tramadol
- Transport stress
- Tumour cell implant into mammary fat pad
- Ulcerative Dermatitis in Mice
- Water quality
- Xenopus laevis
- Zebrafish swabbing


PILOTS
CABIN CREW
GROUND STAFF
AIR TRAFFIC CONTROLLERS

EU / National

Facility

Project

Procedure

https://environment.ec.europa.eu/topics/chemicals/animals-science_en

Animals in science

EU actions for the protection of animals used for scientific purposes

PAGE CONTENTS

https://environment.ec.europa.eu/topics/chemicals/animals-science_en#implementation

Norecopa: PREPARE for better Science

Facility

aaalac INTERNATIONAL

Program Description

A. Animal Care and Use Program

B. Animal environment, Housing and Management

C. Veterinary Care

D. Physical plant

63 pages

www.aaalac.org/program-description

A simple but effective Master Plan

norecopa.no/more-resources/master-plan-and-sops

A Contingency Plan, based upon risk assessment

- Access to emergency services (police, fire, medical and veterinary help, security guards, personnel transport in cases of acute illness)
- Means of communication with staff members at all levels
- SOPs for acute illness, including
  - serious haemorrhages
  - fainting
  - [illegible]
  - corrosive injuries
  - and forms for reporting such injuries
- Firefighting, evacuation of personnel and animals
- Access to specialist services (e.g. ventilation system, plumbing, electrical installations, suppliers of equipment)
- Routines in cases of power failure, water leaks and (if applicable) natural disasters such as flooding
- Routines for emergency killing of animals
- Routines in cases of threats to the facility or personnel

Many of these needed revision in the light of Covid-19
norecopa.no/be-prepared

Temporary staff at weekends and holidays

https://norecopa.no/prepare/6-facility-evaluation/master-plan-and-sops/contingency-plan

Contingency and redundancy

Anything that can go wrong, will go wrong (Murphy's Law)
when it's least convenient *(Sod's Law)*

Work in the spirit of AAALAC,

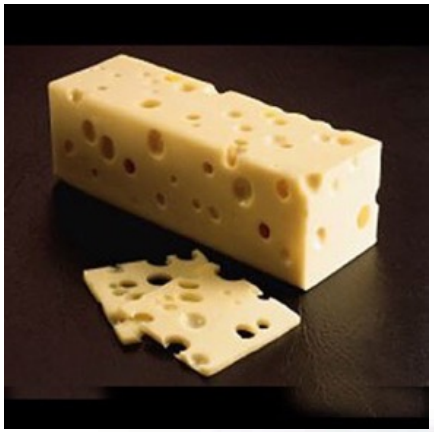
even if not accredited!

Photo: NMBU

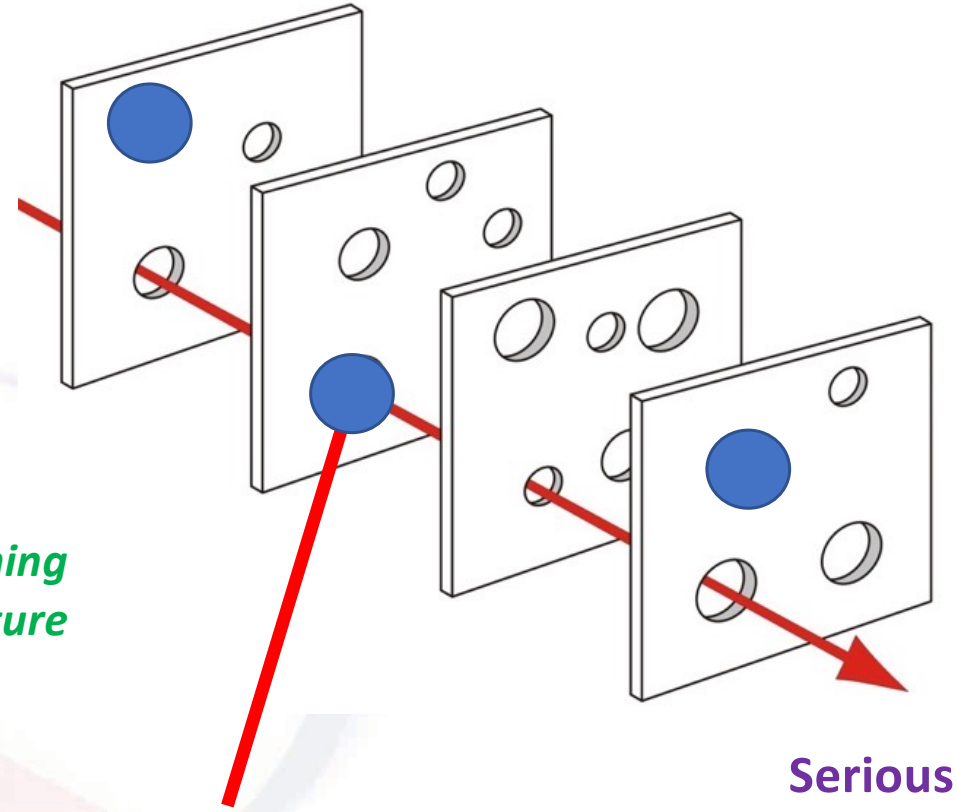
wikipedia


CIRS-LAS Portal
Critical incident reporting system in laboratory animal science
Refine - Reduce - Replace
Homepage
Project
Team
FAQ
Detect a critical incident
Anonymous report
CIRS-LAS.de
Get involved!
We all learn from it!
Expert analysis

“Threat and Error Management”

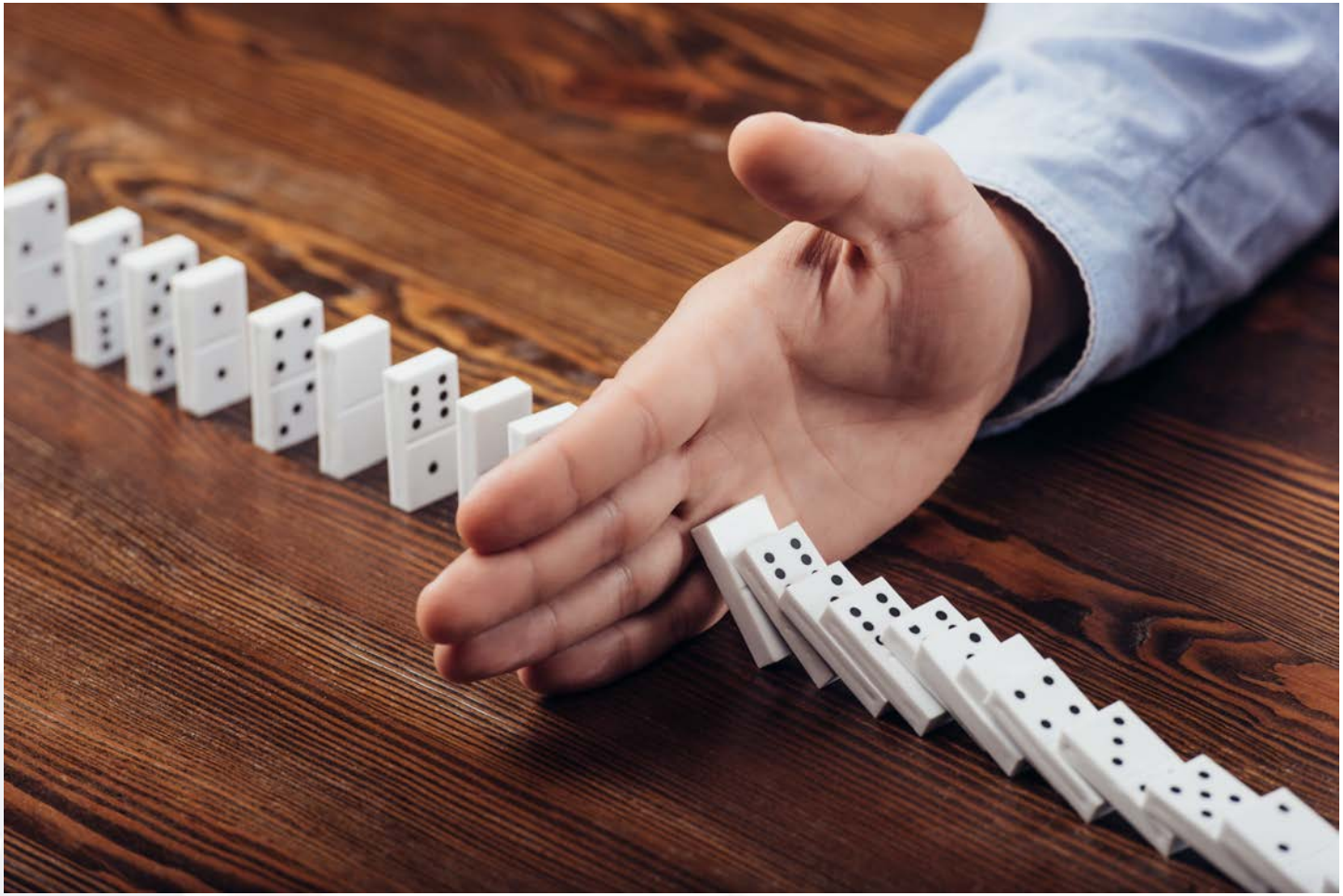


eaugallecheese.com/Swiss-Cheese



wikipedia.org/wiki/Swiss_cheese_model

Embrace the opportunity to learn something from an incident, reducing the risk for future incidents



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Project

A contract between the animal facility and the research group

Division of labour, responsibilities and cost

Clarifying all stages of the experiment

Ensuring that all necessary data are recorded

	Animal facility	Researcher	Not applicable
Animal:			
Arrival date			
Species			
Strain/stock and substrain			
Supplier (full name and address) or bred on the premises			
Number and sex			
Age, weight, stage of life cycle on arrival			
Pre-treatment (surgical or medical) from supplier			
Quality (e.g. SPF, germ-free, gnotobiotic, conventional)			
Acclimation time before the start of the experiment			
Time and duration of fasting (with/without water and bedding)			
Environment:			
Type of housing: barrier/conventional			
Temperature (mean ± variation)			
Light schedule			
Relative humidity (mean ± variation)			
Number of air changes in the animal room/cabinet per hour			
Environmental enrichment			
Housing:			
Free-range, shelf, cabinet, isolator			
Cage type and size			
Number and method of distribution of animals per cage			

Culture of Care

The International Culture of Care Network

norecopa.no/coc

A demonstrable commitment, throughout the establishment, to improving:

- animal welfare
- scientific quality
- care of staff
- transparency for all stakeholders, including the public

It goes beyond simply complying with the law!

Culture of Care facilitates honest discussion

"because we've always done it that way"

"as often as necessary"

"there are no alternatives"

Closely related to a culture of care is

a **Culture of Challenge** (Louhimies, 2015).

Look for the acceptable, rather than choosing the accepted.

The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research

Nathalie Percie du Sert, Viki Hurst, Amrita Ahluwalia, Sabina Alam, Marc T. Avey, Monya Baker, William J. Browne, Alejandra Clark, Innes C. Cuthill, Ulrich Dirnagl, Michael Emerson, Paul Garner, Stephen T. Holgate, David W. Howells, Natasha A. Karp, Stanley E. Lazic, Katie Lidster, Catriona J. MacCallum, Malcolm Macleod, Esther J. Pearl, Ole H. Petersen, Frances Rawle, Penny Reynolds, Kieron Rooney, Emily S. Sena, Shai D. Silberberg, Thomas Steckler, Hanno Würbel

journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.3000410

Version 1 of ARRIVE (2010) was endorsed by more than a thousand journals but only a small number of journals actively enforce compliance

(Swiss study in 2016: 51% of researchers publishing in journals that had endorsed ARRIVE had never heard of them)

'Important information as set out in the ARRIVE guidelines is still missing from most publications sampled:

randomisation 30-30%
blinding 20%
sample size justification <10%
all basic animal characteristics <10%'

'It is likely that the level of resource required from journals and editors currently prohibits the implementation of all the items of the ARRIVE guidelines.'

Laboratory Animals

Laboratory Animals Limited Affiliated Societies

Impact Factor: 2.4
5-Year Impact Factor: 2.5

Restricted access | Review article | First published online September 20, 2023

Twelve years after the ARRIVE guidelines: Animal research has not yet arrived at high standards

Junmin Song, Marco Solmi, Andre F Carvalho, Jae Il Shin, and John PA Ioannidis View all authors and affiliations

OnlineFirst | https://doi.org/10.1177/00236772231181658

journals.sagepub.com/doi/abs/10.1177/00236772231181658

The reproducibility crisis across animal studies jeopardizes the credibility of the main findings derived from animal research, even though these findings are critical for informing human studies. To clarify and improve transparency among animal studies, the ARRIVE reporting guidelines were first announced in 2010 and upgraded to version 2.0 in 2020. However, compliance with and awareness of those reporting guidelines has remained suboptimal. Journal editors should encourage the authors to adhere to those guidelines. Authors, editors, referees, and reviewers should be aware of the ARRIVE guideline 2.0 when assessing and evaluating the methodology and findings of animal studies. However, we should also question whether reporting guidelines alone can change a research culture and improve the reproducibility of animal investigations. Reported research may not reflect actual research. Large segments of animal research efforts are wasted because of poor design choices and because of non-publication rather than suboptimal reporting. Better training of the scientific workforce, interventions at improving animal research at the design stage, registration practices, and alignment of the reward system with the publication of rigorous animal research may achieve more than reporting guidelines alone.

journals.sagepub.com/doi/abs/10.1177/00236772231181658

The ARRIVE guidelines 2.0

This section of the website provides detailed explanations about each item of the guidelines. Use the left-hand side menu to navigate to each item.

To facilitate a step-wise approach to improving reporting, the guidelines are organised into two prioritised sets:

ARRIVE Essential 10

These ten items are the basic minimum that must be included in any manuscript describing animal research. Without this information readers and reviewers cannot assess the reliability of the findings.

Recommended Set

These items complement the Essential 10 set and add important context to the study described. Reporting the items in both sets represents best practice.

arriveguidelines.org

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ARRIVE 2.0

ARRIVE Essential 10		
Study design	1	For each experiment, provide brief details of study design including: a. The groups being compared, including control groups. If no control group has been used, the rationale should be stated. b. The experimental unit (e.g. a single animal, litter, or cage of animals).
Sample size	2	a. Specify the exact number of experimental units allocated to each group, and the total number in each experiment. Also indicate the total number of animals used. b. Explain how the sample size was decided. Provide details of any *a priori* sample size calculation, if done.
Inclusion and exclusion criteria	3	a. Describe any criteria established *a priori* for including and excluding animals (or experimental units) during the experiment, and data points during the analysis. b. For each experimental group, report any animals, experimental units or data points not included in the analysis and explain why. c. For each analysis, report the exact value of N in each experimental group.
Randomisation	4	Describe the methods used: a. To allocate experimental units to control and treatment groups. If randomisation was used, provide the method of randomisation. b. To minimise potential confounding factors such as the order of treatments and measurements, or animal/cage location.
Blinding	5	Describe who was aware of the group allocation at the different stages of the experiment (during the allocation, the conduct of the experiment, the outcome assessment, and the data analysis).
Outcome measures	6	a. Clearly define all outcome measures assessed (e.g. cell death, molecular markers, or behavioural changes). b. For hypothesis-testing studies, specify the primary outcome measure, i.e. the outcome measure that was used to determine the sample size.
Statistical methods	7	a. Provide details of the statistical methods used for each analysis. b. Specify the experimental unit that was used for each statistical test. c. Describe any methods used to assess whether the data met the assumptions of the statistical approach.
Experimental animals	8	a. Provide details of the animals used, including species, strain and substrain, sex, age or developmental stage, and weight. b. Provide further relevant information on the provenance of animals, health/immune status, genetic modification status, genotype, and any previous procedures.
Experimental procedures	9	For each experimental group, including controls, describe the procedures in enough detail to allow others to replicate them, including: a. What was done, how it was done and what was used. b. When and how often. c. Where (including detail of any acclimation periods). d. Why (provide rationale for procedures).
Results	10	For each experiment conducted, including independent replications, report: a. Summary/descriptive statistics for each experimental group, with a measure of variability where applicable. b. If applicable, the effect size with a confidence interval.

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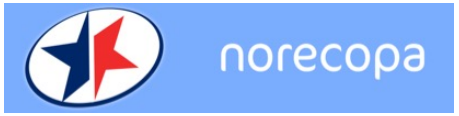

ARRIVE 2.0

Recommended Set		
Abstract	11	Provide an accurate summary of the research objectives, animal species, strain and sex, key methods, principal findings, and study conclusions.
Background	12	a. Include sufficient scientific background to understand the rationale and context for the study, and explain the experimental approach. b. Explain how the animal species and model used address the scientific objectives and, where appropriate, the relevance to human biology.
Objectives	13	Clearly describe the research question, research objectives and, where appropriate, specific hypotheses being tested.
Ethical statement	14	Provide the name of the ethical review committee or equivalent that has approved the use of animals in this study and any relevant licence or protocol numbers (if applicable). If ethical approval was not sought or granted, provide a justification.
Housing and husbandry	15	Provide details of housing and husbandry conditions, including any environmental enrichment.
Animal care and monitoring	16	a. Describe any interventions or steps taken in the experimental protocols to reduce pain, suffering and distress. b. Report any expected or unexpected adverse events. c. Describe the humane endpoints established for the study and the frequency of monitoring.
Interpretation /scientific implications	17	a. Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature. b. Comment on the study limitations including potential sources of bias, limitations of the animal model, and imprecision associated with the results.
Generalisability /translation	18	Comment on whether, and how, the findings of this study are likely to generalise to other species or experimental conditions, including any relevance to human biology (where appropriate).
Protocol registration	19	Provide a statement indicating whether a protocol (including the research question, key design features, and analysis plan) was prepared before the study, and if and where this protocol was registered.
Data access	20	Provide a statement describing if and where study data are available.
Declaration of interests	21	a. Declare any potential conflicts of interest, including financial and non-financial. If none exist, this should be stated. b. List all funding sources (including grant identifier) and the role of the funder(s) in the design, analysis and reporting of the study.

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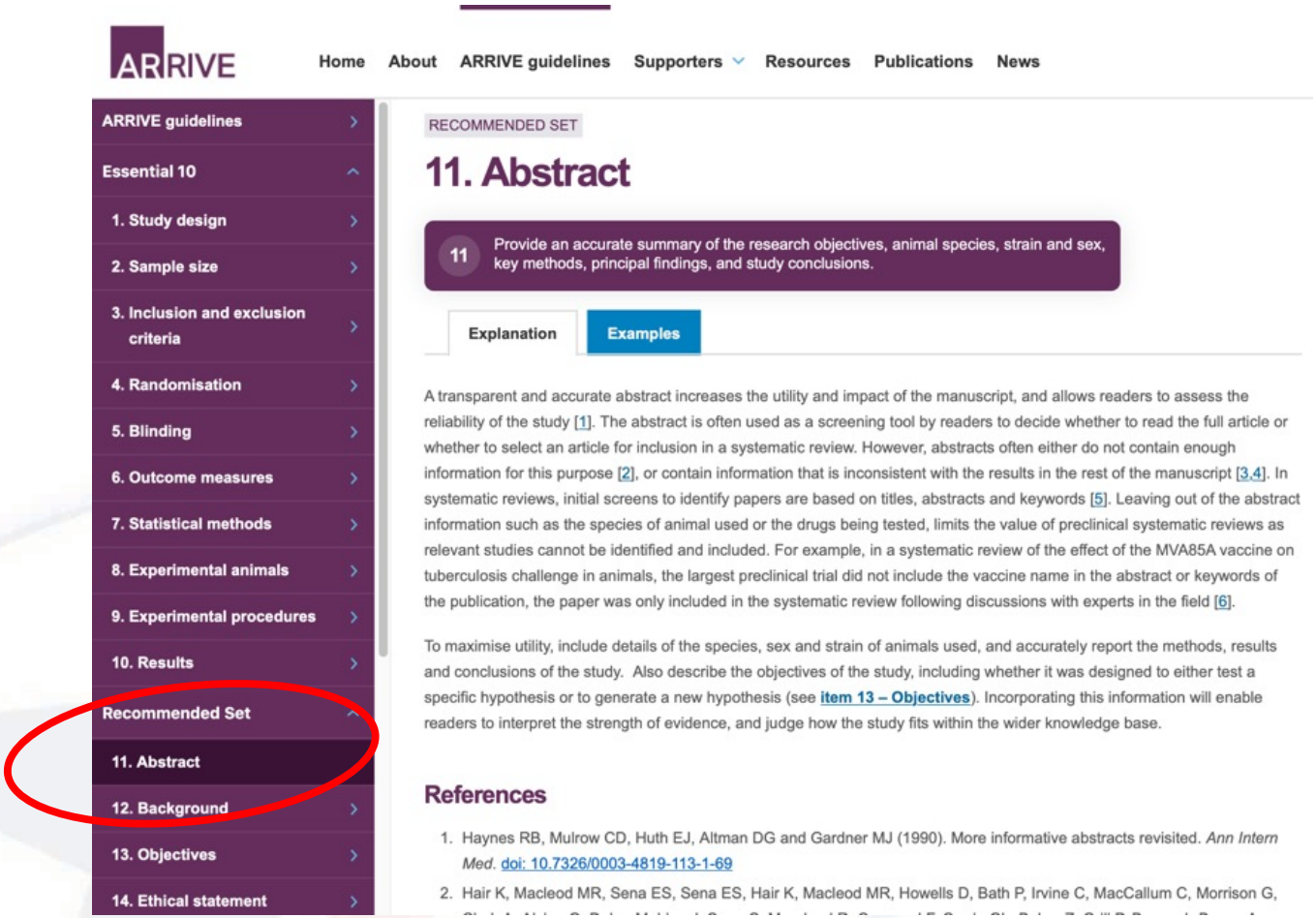
arriveguidelines.org



There are three broad areas which need to be considered when planning animal studies:

1. The suitability of the species or strain as a model of the target organism
2. The ethical issues surrounding their use: 'choosing the right animal for the right reason'. The large increase in use of genetically altered lines has created increasing concern about the suitability of these animals as models of human conditions.
3. Characterisation of the animals. Items to be considered, in collaboration with the supplier, include:
   - Species, strain, line and phenotype (with an explanation of any genetic modifications)
   - Age, developmental stage, sex and weight
   - Stage of oestrous cycle and any previous breeding history
   - Any necessary pre-treatment (e.g. castration for this
   - Name and address of the supplier/breeder, method of capture and transport
   - Health status (e.g. germ-free, gnotobiotic, SP
   - Re-use of animals, which should be justified legislation
   - Any plans for release or re-homing, which m

More resources

- Examples and references from the NC3Rs
- Information on inbred strains of mice and rats
- Strategies to minimise genetic drift and maximise experimental reproducibility in mouse research
- Mouse Locator, UK
- The Collaborative Cross panel of inbred mouse strains
- Nude mice - more than what meets the eye
- The Rat Guide
- Rat Behavior and Biology

Norecopa: PREPARE for better Science

norecopa

"We ARRIVED, because we were PREPARED"

- ✓ *Better Science*
- ✓ *Improved animal welfare*
- ✓ *Advancement of the 3Rs*
- ✓ *Safer working environment*

Norecopa: PREPARE for better Science

We can work to tip the balance

***The 3 Rs* to minimise the harm:**

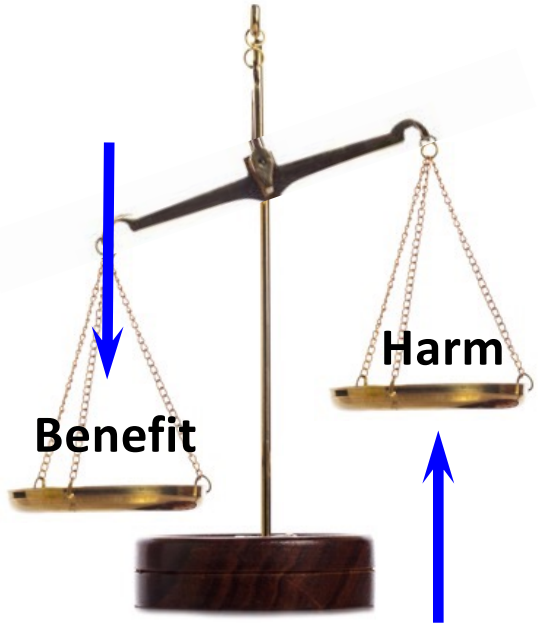
- *Replace the unnecessary experiments*
- *Reduce the number of animals used*
- *Refine the conditions for the animals*

***The 3 Ss* - your commonsense and your heart**

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

***The 3 Vs* to increase the validity of the experiment:**

- *Construct Validity (can the model answer the question?*
- *Internal Validity (has the experiment been correctly designed?)*
- *External Validity (are the results translatable to the target group?)*



norecopa.no/3R
norecopa.no/3S
norecopa.no/3V

norecopa.no/poster

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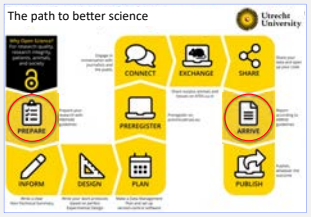
Adrian Smith, Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 64, 1431 Ås, Norway
adrian.smith@norecopa.no

What's the problem?

Preclinical *in vivo* research needs to be reproducible and translatable, while maximising the animals' welfare and replacing them with alternatives wherever possible. This can be summed up in **the 3Rs** of Russell & Burch: ***Replace, Reduce & Refine***.

Scientists are usually well aware of ***reporting*** guidelines when publishing research. These are important, but a sub-standard study, like a burnt cake, cannot be improved by a better description. Guidelines for ***planning***, although not mandatory, are of great help in designing better experiments.



norecopa.no/PREPARE

What can Norecopa offer?

Norecopa maintains a comprehensive database of resources for scientists, which include:

- over 9,000 searchable webpages of quality 3R resources, with filters to facilitate searching
- the PREPARE guidelines for planning animal experiments, with a checklist in over 30 languages
- links to recordings of webinars covering all aspects of animal research
- an International Webinars & Meetings Calendar
- a collection of over 400 guidelines for planning and conducting animal research
- an English-language newsletter with the latest developments within the 3Rs
- the NORINA database of alternatives to animal use in education and training
- a slide set describing the 3R concept in detail: norecopa.no/3Rs
- a Refinement Wiki

Examples of Norecopa's resources:

PREPARE covers:

- ✓ *Formulation of a study*
- ✓ *Dialogue between scientists and the animal facility*
- ✓ *Quality control of the components in the study*

norecopa.no/PREPARE

The Refinement Wiki
wiki.norecopa.no

Norecopa gratefully acknowledges financial support from:
The Norwegian Parliament, the Ministry of Agriculture & Food and the Ministry of Trade, Industry & Fisheries; the Nordic Society against Painful Experiments (NSMSD), Novo Nordisk, the Norwegian Animal Protection Alliance (Dyrevernalliansen), the Norwegian Society for Protection of Animals (Dyrebeskyttelsen Norge), the Research Council of Norway, Laboratory Animals Ltd., the Royal Society for the Prevention of Cruelty to Animals (RSPCA), Sanofi, the Scottish Accreditation Board, the Stiansen Foundation, the Universities Federation of Animal Welfare (UFAW) and the US Department of Agriculture (USDA).
Toolbox graphic: colourbox.com

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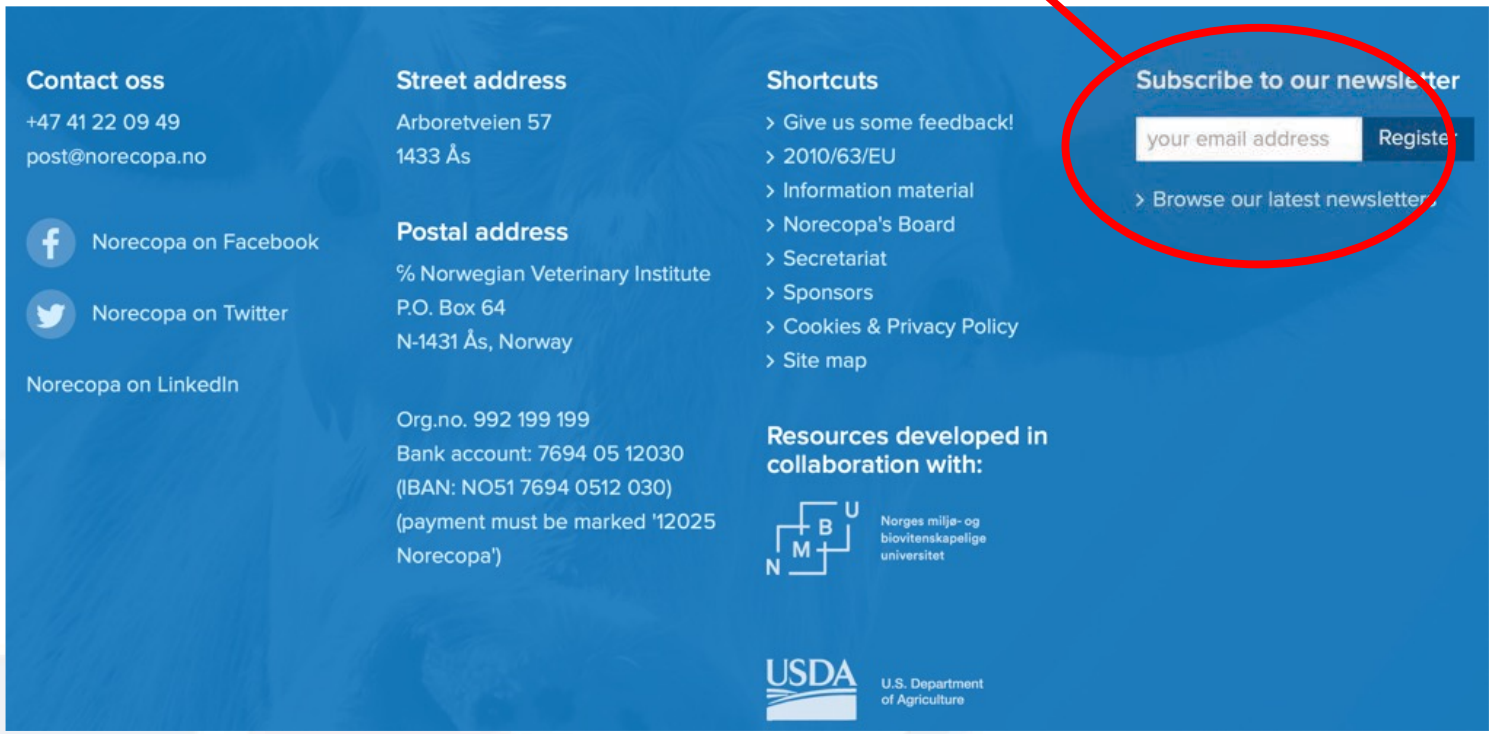
Architect Finn Rahn's Legacy
Laboratory Animals Ltd.
Nordic Society Against Painful Experiments (NSMSD)
Norwegian Society for Animal Protection (Dyrebeskyttelsen Norge)
Norwegian Animal Protection Alliance (Dyrevernalliansen)

Novo Nordisk
Royal Society for the Prevention of Cruelty to Animals (RSPCA)
Sanofi
Scottish Accreditation Board (SAB)
Stiansen Foundation
Universities Federation for Animal Welfare (UFAW)
US Department of Agriculture (USDA)

Graphics: colourbox.com

norecopa.no/NRW

English-language newsletters



Thank you for listening!