Norecopa: PREPARE for better Science

Adrian Smith

adrian.smith@norecopa.no @adrian_3r

norecopa.no/121222



https://norecopa.no

Norway's National Consensus Platform for the

Three Rs: Replacement, Reduction and Refinement

and a source of *global* 3R resources



Established in 2007

Slide deck about the 3Rs



The 3Rs of Russell and Burch:

Replacement, Reduction & Refinement

Adrian Smith

adrian.smith@norecopa.no
 @adrian_3r

With some material from:

Smith AJ & Richmond J (Forthcoming). 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.

Available at norecopa.no/3Rs

version 18.11.22 09.00 CET







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!

Communication and the Culture of Care

Penny Hawkins, RSPCA Research Animals Department on behalf of the International Culture of Care Network'

essential for a good Culture of Care

Here are some examples from International Culture of Care network members

Regular meetings

Scheduled meetings for scientists, animal

technologists, vets, unit managers and AWERB members

Regular refresher/update meetings for all organise

Special events Duo-talks: researcher talks

about their science, and animal technologists talk about techniques and anin care within the project

ELH organises an informal meeting for all, in which anyone can raise welfare



Building communication into existing processes

Each study has a prestart and wash-up meeting involving everybody

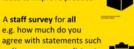
Three Rs improvements reported to AWERB & shared at external user

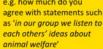


e.g. how much do you animal welfare

Other ideas

A 'boxless' event: anyone can submit 'out of the box' ideas to improve practice













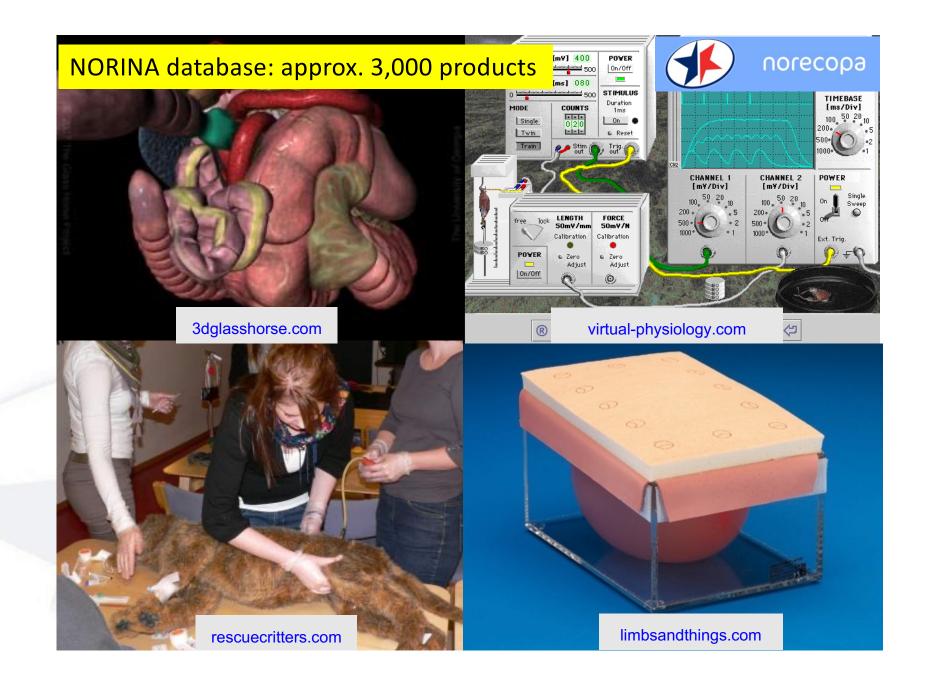
norecopa.no: an updated overview of global 3R resources



Design and reporting of animal experiments

This page supplements advice given in <u>Section 4 of the PREPARE guidelines</u>. PREPARE covers all aspects of design (including animal and facility related issues).





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

Testing anaesthetic depth in the chicken

Norecopa 598 views





Rat s.c. injection Norecopa 1,380 views



ANATOMÍA DE LA RAT

Rat i.p. injection (method 2) Norecopa 1,280 views

Anatomia de la rata Norecopa 977 views



Blood collection from the saphenous vein in the mouse



Subcutaneous injection in the rat - Technique 1 Norecopa 2,249 views





Intravenous injection in a rabbit Norecopa 2,025 views



Lifting a rabbit Norecopa 2,420 views



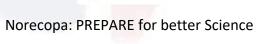
Subcutaneous injection in the rabbit Norecopa 1,479 views



Subcutaneous injection in the chicken Norecopa 1,806 views



Immobilisation of the rabbit Norecopa 2,072 views





Blood san

Blood san



researchanimaltraining.com

Articles v eModules v Log in

Training resources for animal research



National Legislation (EU1)

Understand the national and international legal and regulatory framework within which projects involving animals are constructed and managed and of the legal responsibilities of the people involved.



Ethics, Animal Welfare and the 3Rs (EU2)

Identify the ethical and welfare issues raised by the use of animals in scientific procedures and understand the basic principles of the 3Rs.



Basic and Appropriate Biology (EU3)

Discover the basic principles of animal behaviour, care, biology and husbandry.



Animal Care, Health and Management (EU4)

Examine information on various aspects of animal health, care and management including, environmental controls, husbandry practices, diet, health status and disease.



Recognition of Pain, Suffering and Distress (EU5)

Identify the normal condition and behaviour of experimental animals and differentiate between a normal animal and one which is showing signs of pain, suffering or distress.



Minor Procedures without Anaesthesia (EU7)

An introduction to the theory relating to minor procedures and information about appropriate methods of handling, restraint, appropriate techniques for injection, dosing and sampling relevant to the species.



Humane Methods of Killing (EU6.1) Learn the principles of humane killing

including descriptions of the different methods available and information to help you compare the methods permitted to determine the most appropriate method.



Anaesthesia for Minor Procedures (EU20)

Guidance and information for individuals. who, during their work with animals, will need to apply sedation or short-term anaesthesia for a brief period and mild pain level procedure.

eModules



eModule - Recognition and Prevention of Pain, Suffering and Distress (EU5)



eModule – Humane Methods of Killing (EU6)



eModule - Design of procedures and projects (level 1) (EU10)



eModule - Design of procedures and projects (level 2) (EU11)



eModule - The Severity Assessment Framework (EU12)



eModule - Anaesthesia for Minor Procedures (EU20)



eModule - Pre-Anaesthetic Preparations (EU21-1)



eModule - Choosing an Anaesthetic (EU21-2)



eModule - Anaesthetic Monitoring and Intraoperative Care (EU21-



eModule - Anaesthetic Breathing Systems, Airway Management and Neuromuscular Blocking Agents (EU21-4)



eModule - Anaesthetic Management and Preventing Problems (EU21-



eModule - Post Anaesthetic Care (EU21-6)



eModule - Project Evaluation (EU25)



TextBase:

1,500 books related to LAS:

norecopa.no/textbase

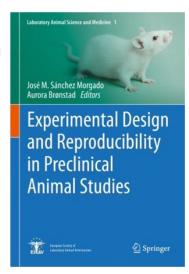
Experimental Design and Reproducibility in Preclinical Animal Studies

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.



norecopa.no/textbase/experimental-design-and-reproducibility-in-preclinical-animal-studies

3R-Guide (400 guidelines for animal research and testing)



norecopa.no/3r-guide



Guidance on the severity classification of procedures involving fish

Report from a Working Group convened by Norecopa

Laboratory Animals, 2011 norecopa.no/categories



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

norecopa.no/PREPARE/prepare-checklist







The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

Adrian J. Smith*, R. Eddie Clutton*, Elliot Lilley*, Kristine E. Aa. Hansen* & Trond Brattelid*

"Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oxlo, Norwey; "Royal (Dick) School of Veterinary Studies, Easter Bush, Miderbian, EHSS 9RG, U.K.; Research Animais Department, Science Group, RSPCA, Wilberforce Way, Susthmater, Horsham, West Sussex, RH13 9RS, U.K.;
"Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Normeplan University of Life Sciences, P.O. Bax 8146 Dep., 0033 Oslo, Nanuay; "Division for Research Management and External Funding, Western Nanuay University of Applied Sciences, 5020 Bergen, Norway.

PREPARE' consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE². 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 Consider the use of systematic reviews Dedde upon databases and information Assess the relevance of the species to b questions with the least suffering, and its Assess the reproducibility and translatable
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-be nefit 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 #pslacement, 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.
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.





Recommen dation

 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 prepara 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 ne 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 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 affer 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
ior	s much information as possible about test substances. the feasibility and validity of test procedures and the skills needed to perform them.
sior	the feasibility and unlittly of test procedures and the skills needed to perform them
SIOT 11. Quarantee and health monitoring	the feasibility and validity of test procedures and the skills needed to perform them. In the characteristics of the animals that are essential for the study and for reporting.
11. Quarantine and	the feasibility and validity of test procedures and the skills needed to perform them. In the characteristics of the animals that are essential for the study and for reporting ation of surplus animals.
11. Quarantine and health monitoring	the feasibility and validity of test procedures and the skills needed to perform them. In the characteristics of the animals that are essential for the study and for reporting, sation of surplus animals. Discuss the animals' likely health status, any needs for transport, quarantine and isolation, health monitoring and consequences for the personnel. 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). Develop refined procedures for capture, immobilisation, marking, and release or rehoming.
11. Quarantine and health monitoring 12. Housing and husbandry 13. Experimental procedures 14. Humane killing.	the feasibility and validity of test procedures and the skills needed to perform them. In the characteristics of the animals that are essential for the study and for reporting, action of surplus animals. Discuss the animals' likely health status, any needs for transport, quarantine and isolation, health monitoring and consequences for the personnel. Attend to the animals' specific instincts and needs, in collaboration with expert staff. Discuss acclimatization, optimal housing conditions and pocedures, environmental factors and any experimental limitations on these (e.g. food deprivation, solitary housing). Develop refined procedures for capture, immobilisation, marking, and release or rehoming. Develop refined procedures to rapture, immobilisation, sampling, sedation and ansesthesis, surge and other techniques.
11. Quarantine and health monitoring 12. Housing and husbandry 13. Experimental procedures	the feasibility and validity of test procedures and the skills needed to perform them. In the characteristics of the animals that are essential for the study and for reporting, sation of surplus animals. Discuss the animals' likely health status, any needs for transport, quarantine and isolation, health monitoring and consequences for the personnel. 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). Develop refined procedures for capture, immobilisation, marking, and release or rehoming. Develop refined procedures to capture, immobilisation, sampling, sedation and anaesthesis, surge and other techniques.

- 1. Smith AJ, Clutton RE, Lilley E, Hansen KEA & Brattelld T. PREPARE Guidelines for Planning Animal Research and Testing.
- Labora bry Animals, 2017, DOI: 10.1177/0023677217724823.

 2. Klikenry 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





In addition to the checklist, much more information is available on:

norecopa.no/PREPARE





norecopa.no/PREPARE

- 3-Ethical issues, harmbenefit assessment and humane endpoints
- 3a Construct a lay summary.
- 3b In dialogue with ethics committees, consider whether statements about this type of research have already been produced.
- 3c Address the 3Rs (Replacement, Reduction, Refinement) and the 3Ss (Good Science, Good Sense, Good Sensibilities).

- 5. Have the experiments been carried out before, and is any repetition justifiable?
- 6. What approaches to reduce distress r have been considered?



 Have national or local research ethics committees already produced statements relevant to the research being planned? Consideration should also be paid to the broader context of the research. For example, research directed at increasing the productivity of farming at the expense of (or without improving) individual animal welfare, or wildlife research whose primary aim is population management.

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

nd will any advances in this ses only index the title and rejected?

- Assessment and justify any likely
 - Discuss the learning objectives, if the animal use is for educational or training purposes.
 - Allocate a severity classification to the project.
 - 3h Define objective, easily measurable and unequivocal humane endpoints.
 - 3i Discuss the justification, if any, for death as an end-point.
 - 4-Experimental design and statistical analysis

- 3. Have the Three S's (Good Science, Good Sense and Good Sensibilities 2) been addressed? Sufficient time should be allocated to this point, since two of the three S's are highly subjective, but equally important. The use of commonsense and critical anthropomorphism are justifiably part of the work to assess the impact of research on animals, not least when a scientific evidence base does not exist.
- 4. Does the proposed study have a clear rationale and scientific relevance, and what will be the next step if the hypothesis is supported or rejected?
- 5. Have the experiments been carried out before and is any repetition justifiable?
- 6. What approaches to reduce distress rather have been considered?
- 7. Will the preject undergo pre-registration and will pogative results be published, to avoid publication bias?

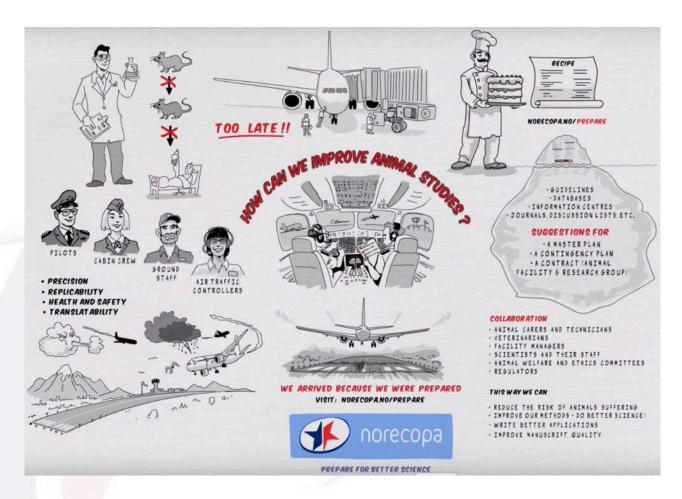
Many more links to resources on ethics are available here ♂.

Details also ut pre-registration of animal studies and reporting of critical incidents are to be found in the section on Experimental Design and Statistical Analysis (2).

Harm-Benefit Assessment

norecopa.no/PREPARE/film

3-minute cartoon film





norecopa.no / Meetings / Meetings Calendar

norecopa.no/meetings/meetings-calendar

Webinar and Meetings calendar

- ► The influence of age on experimental outcomes and animal care , webinar (Paul Potter), 29 November 2022
- ▶ SGV 2022 Meeting (Swiss Laboratory Animal Science Association) , Lausanne, 29-30 November 2022

+ webpages for recorded meetings, sorted by PREPARE topics

December 2022

December 2022

- ► How can alternatives to animal testing bring benefit to chemical industry , webinar (Barbara Birk), 1 December 2022
- ▶ Replacement methods for the diagnostics of botulinum neurotoxins: Challenges and recent progress , webinar (Brigitte Dorner), 1 December 2022
- The culture of care within the Directive 2010/63/EU ☑, webinar (Susanna Louhimies), 2 December 2022



The Refinement Wiki



wiki.norecopa.no

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

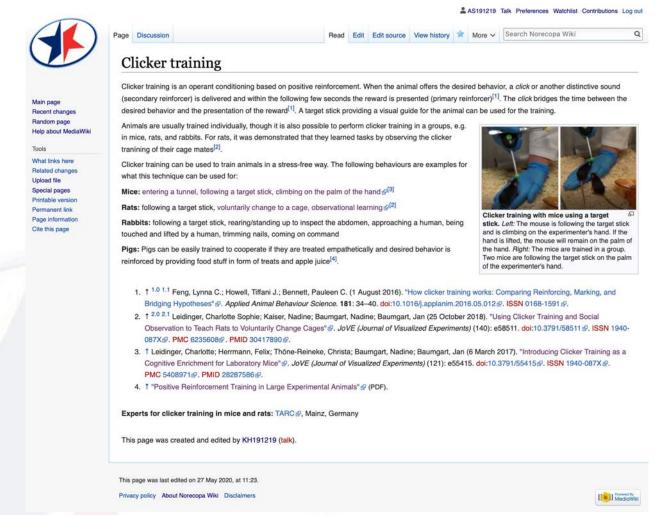
Designed to be

- 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



wiki.norecopa.no



All Wiki content is also retrievable from Norecopa's search engine

A simple instruction manual to keep the threshold for adding new content as low as possible

CAPCITITION

This page supplements advice given in <u>Section 4 of the PREPARE guidelines</u>. PREPARE covers all aspects of design (including animal and facility related issues).



Pages created (December 2022)

wiki.norecopa.no



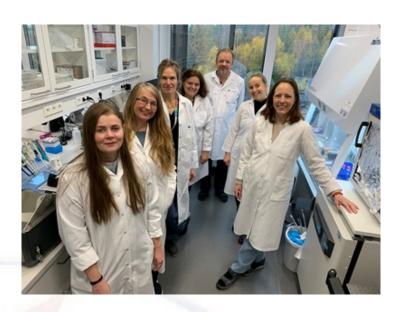
- Acclimatisation
- Adrian Smith
- Alphaxalone
- Anaesthesia in neonates
- Analgesia
- Asepsis
- · Blood sampling of hamsters
- Blood sampling of pigs
- Blood sampling of rainbow trout
- · Breeding strategies for mice
- Clicker training
- Contingency plans
- Decapitation
- Detecting early onset of clinical 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

Norecopa's 3R Prize 3,000 euros + Diploma







Biomarkers and bioassays for veterinary research

- fish gill cell cultures
- Norwegian Veterinary Institute



Sponsorship



Online PREPARE course, January 2023



Training to deliver rigorous and reproducible animal studies by planning in accordance with the PREPARE guidelines.

Norecopa: PREPARE for better Science



Culture of Care meeting



FRAME Training School, Bergen, March 2023





Let's PREPARE together to ARRIVE in better shape: how to plan animal experiments

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

The Refinement Wiki wiki.norecopa.no

What can Norecopa offer?

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



- 8,900 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 400 guidelines for planning and conducting animal research
- an English-language newsletter with the latest developments within experimental design
- the NORINA database of alternatives to animal use in education and training
- a Refinement Wiki

Examples of Norecopa's resources:



Norecopa gratefully acknowledges financial support from:

The Missengian Resistances, the Admitty of Agriculture & Food and the Ministry of Trade, Industry & Finderics: the Next Sciencies against Residul Equiriment (INSMS), Noo-Ministry, of Trades in New York (Institute of Agriculture & Finderics), the Next Science of New York (Institute of New York (Ins

Norecopa: PREPARE for better Science

norecopa.no/Europhysiology



norecopa

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SHARE THE NEWSLETTER ON F I I III

Newsletter no. 3-2022 from Norecopa

Welcome to Norecopa's third newsletter in 2022!

Please share this newsletter with your colleagues and friends!

Norecopa maintains an international Webinars and Meetings Calendar [7], which is updated several times a week, with links to recorded webinars and events here

You will find shortcuts to several other key resources on our front page .

We continue to maintain a list of resources related to the Covid-19 pandemic and about preparedness in general: Be PREPAREd [... Let us know if you have additions.

You can tip a friend, subscribe or unsubscribe, and share the newsletter on social media using the links above. We are on Facebook [7], Twitter [7] and LinkedIn [7].

All Norecopa's newsletters can be read here and their content is indexed by the search

This newsletter contains the following items (if some links do not work, check that your mail program has opened the whole of the newsletter):

- ews from other 3R Centres

- mpses from research

English-language newsletters

norecopa.no/news/newsletters

7-8 times a year

1,200 international subscribers



At the bottom of Norecopa's webpages

English-language newsletters



norecopa.no/121222