Organizacijska reforma:
definiranje razina odgovornosti i zadataka

Radionica/Workshop

Presentation created and delivered by:

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Sveučilište u Splitu, Medicinski fakultet

03. srpnja 2020.

Radionica će biti foto-dokumentirna

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Europska unija
Zajedno do fondova EU

EUROPSKI STRUKTURNI
I INVESTICIJSKI **FONDOVI**

Operativni program
**KONKURENTNOST
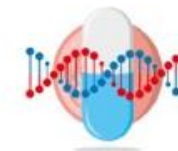I KOHEZIJA**

REPUBLIKA HRVATSKA
Ministarstvo regionalnoga razvoja
i fondova Europske unije

Projekt *"Stavljanje u funkciju novoizgrađene nastambe za pokusne životinje na Sveučilištu u Splitu"*

O projektu:

- Ukupna vrijednost projekta: 19 214 337.50 kn
  Iznos koji sufinancira EU: 17 996 047.92 kn
  Razdoblje provedbe projekta: veljača 2019. - studeni 2020.

- Prijavitelj: Sveučilište u Splitu

- Partner: Medicinski fakultet u Splitu

- Projekt sufinancira Europska unija iz Europskog fonda za regionalni razvoj.

Elementi projekta:

Element 1. ADAPTACIJA PROSTORA NASTAMBE ZA ŽIVOTINJE

Element 2. OPREMANJE PROSTORA NASTAMBE

Element 3. **ORGANIZACIJSKA REFORMA**

PROMIDŽBA I VIDLJIVOST, UPRAVLJANJE PROJEKTOM I ADMINISTRACIJA

EUROPSKI STRUKTURNI I INVESTICIJSKI **FONDOVI**

Europska unija
Zajedno do fondova EU

Operativni program
KONKURENTNOST I KOHEZIJA

REPUBLIKA HRVATSKA
Ministarstvo regionalnoga razvoja
i fondova Europske unije

Operationalization of newly-built facility for experimental animals at the University of Split

KK.01.1.1.02.0026
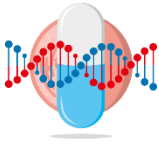
Co-financed by European Union, EU Regional Development Fund.

- Call: Investment in the reorganization of processes and infrastructure in the field of research, development and innovation.

Total project value: 19.214.337,50 HRK (~2.5M€)
Total EU Grants: 17.996.047,92 HRK (~2.4M€)
Project Implementation Period: February 2019 - November 2020.
Applicant/Project user: University of Split
Project partner: University of Split, School of Medicine
Web:

Legal and ethical framework setting the animal research field
(models for Good Research Practice)

Directive 2010/63/EU*
of the European Parliament and
of the Council of 22nd September 2010 on the protection of animals used
for scientific purposes

Annex III of the Directive dictates the minimal requirements for care and accommodation of animals, in Appendix A of the European Convention ETS 123

*Transposition into National legislation (NN 55/13),

subsequent changes 2017, 2019

National Competent Authority (NCA)_Ministry of Agriculture

Ministarstvo Poljoprivrede

Uprava za veterinarstvo i sigurnost hrane

http://veterinarstvo.hr

Dobrobit životinja za pokuse

Pravilnik o zaštiti životinja koje se koriste u znanstvene svrhe

Council of Europe

- European Treaty Series No. 123: **ETS 123,** European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes, **Appendix A**

- **Guidelines for accommodation and care of animals**

(these minimum cage sizes are generally bigger then housing density recommendations in *the Guide*)

Table A.1. Mice: Minimum enclosure dimensions and space allowances

	Body weight (g)	Minimum enclosure size (cm²)	Floor area per animal (cm²)	Minimum enclosure height (cm)
In stock and during procedures	up to 20 over 20 to 25 over 25 to 30 over 30	330 330 330 330	60 70 80 100	12 12 12 12
Breeding		330 For a monogamous pair (outbred/inbred) or a trio (inbred). For each additional female plus litter 180 cm² should be added.		12
Stock at breeders* Enclosure size 950 cm²	less than 20	950	40	12
Enclosure size 1500 cm²	less than 20	1500	30	12

* Post-weaned mice may be kept at these higher stocking densities, for the short period after weaning until issue, provided that the animals are housed in larger enclosures with adequate enrichment. These housing conditions should not cause any welfare deficit such as: increased levels of aggression, morbidity or mortality, stereotypies and other behavioural deficits, weight loss, or other physiological or behavioural stress responses.

Table A.2. Rats: Minimum enclosure dimensions and space allowances

	Body weight (g)	Minimum enclosure size (cm²)	Floor area per animal (cm²)	Minimum enclosure height (cm)
In stock and during procedures*	up to 200 over 200 to 300 over 300 to 400 over 400 to 600 over 600	800 800 800 800 1 500	200 250 350 450 600	18 18 18 18 18
Breeding		800 Mother and litter. For each additional adult animal permanently added to the enclosure add 400 cm²		18
Stock at breeders** Enclosure size 1500 cm²	up to 50 over 50 to 100 over 100 to 150 over 150 to 200	1500 1500 1500 1500	100 125 150 175	18 18 18 18
Stock at breeders** Enclosure size 2500 cm²	up to 100 over 100 to 150 over 150 to 200	2500 2500 2500	100 125 150	18 18 18

AAALAC-I performance-based
Primary Standards (free on-line access)

- ***Guide for the Care and Use of Laboratory Animals*** *(The Guide)*

National Research Council 2011, the 8th edition

- Guide for the Care and Use of Agricultural Animals in Research and Teaching (Ag Guide), FASS 2010

- European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, Council of Europe

(ETS 123)

in vivo research stakeholders
(from cage to bedside)

- **Laboratory animals**

- Animal Facility users (*in vivo* research teams_researcher, practitioners_animal care takers, technicians, manager, etc)

- Regional and global collaborators - MefST suradne institucije

- Sponsors (funders), scientific journals, publishers

- Patent office

- Registered breeders, users (registrirani korisnici e.g. akademija, industrija)

- National Competent Authorities_NCA e.g. Zakonodavna tijela (EU, nacionalna, Ministarstvo poljoprivrede-veterinarska inspekcija, Ministarstvo rada i mirovinskog sustava, Uprava za rad i zaštitu na radu, Ministarstvo znanosti i obrazovanja, njihove inspekcijske službe)

- National ethical committee, institutional ethical committee

- Animal protection organisations (organizacije za zaštitu životinja na pr. Prijatelji životinja)

- National and international expert associations, e.g. LAS _CROLASA, FELASA, ICLAS, AAALAC, ECLAM, ESLAV , they publish "expert working group recommendations and standards", also LASM specialist fields guidelines

- **Patients**

4.6. Naziv projekta:

4.6.1. Namjena i ciljevi projekta (*navesti/zaokružiti odgovarajuće*):

1) temeljna istraživanja

2) translacijska ili primijenjena istraživanja s bilo kojom od sljedećih namjena:

    a. zaštita, prevencija, dijagnosticiranje ili liječenje bolesti, lošeg zdravstvenog stanja ili drugih nepravilnosti (promjena nastalih zbog bolesti) ili njihovih učinaka kod ljudi, životinja ili biljaka

    b. ocjena, otkrivanje, reguliranje ili promjena fizioloških stanja kod ljudi, životinja ili biljaka ili

    c. dobrobit životinja i poboljšanje proizvodnih uvjeta za životinje koje se uzgajaju i drže za poljoprivredne potrebe

3) bilo koje namjene iz točke 2. ovoga stavka pri razvoju, proizvodnji ili ispitivanju kvalitete, učinkovitosti i sigurnosti lijekova, prehrambenih proizvoda i hrane za životinje te drugih tvari ili proizvoda

4) zaštita prirodnog okoliša radi zaštite zdravlja ili dobrobiti ljudi ili životinja

5) istraživanja usmjerena na zaštitu životinjskih vrsta

6) za potrebe visokoškolskog obrazovanja ili izobrazbe za stjecanje, održavanje ili unapređivanje strukovnih vještina

7) forenzička ispitivanja.

Functions and specific tasks under 2010/63/EU:
designated vet, principal investigator (project lead_scientist_researcher), animal welfare officer, training officer, NCA liaison, technician, animal caretaker, surgeon etc

Table 1. Mapping of modules to Functions and specific tasks.

EU ID	Module description	EU Function A	B	C	D[a]	Species specific
1	National legislation	C	C	C	C	
2	Ethics, animal welfare and the 3Rs (level 1)	C	C	C	C	
3.1	Basic and appropriate biology	C	C	C	C	Yes
4	Animal care, health and management	C	C	C	C	Yes
5	Recognition of pain, suffering and distress	C	C	C	C	Yes
6.1	Humane methods of killing	C	C	C	C	Yes
3.2	Basic and appropriate biology – skills	F		F	F	Yes
7	Minimally invasive procedures without anaesthesia	F	F			Yes
8	Minimally invasive procedures without anaesthesia – skills	F				Yes
9	Ethics, animal welfare and the 3Rs (level 2)		F			
10	Design of procedures and projects (level 1)	T	F			
11	Design of procedures and projects (level 2)		F			
6.2	Humane methods of killing – skills	T		T	F	Yes
20	Anaesthesia for minor procedures	T	T			
21	Advanced anaesthesia for surgical and prolonged procedures	T	T			
22	Principles of surgery	T	T			
23	Advanced animal husbandry, care and enrichment practices			T		

EU Function A: carrying out procedures on animals; EU Function B: designing procedures and projects; EU Function C: taking care of animals; EU Function D: killing animals. Level 1: At this level the trainee should describe and explain the subjects taught; level 2: at this level the trainee should show detailed understanding and should be able to critically evaluate the subjects taught.
[a]Module 6.3 is a stand-alone module for EU Function D (not mentioned here).
C: core modules; modules that are required for all Functions; F: function-specific (prerequisite) modules; T: task-specific modules: modules that are relevant to specific tasks within a Function

ECCVT (European Coordinating Committee on Veterinary Training)
"day-one-competencies" for laboratory animal veterinarian
(VetCEE-Veterinary Continuous Education in Europe i.e.
LAS dossier of competencies for academic training programmes)

Working Party Report

ESLAV/ECLAM/LAVA/EVERI recommendations for the roles, responsibilities and training of the laboratory animal veterinarian and the designated veterinarian under Directive 2010/63/EU

G M Poirier[1], C Bergmann[2], D G Denais-Lalieve[3], I A Dontas[4],
N Dudoignon[5], H Ehall[6], J M Fentener van Vlissingen[7],
M Fornasier[8], R Kalman[9], A Hansen[10], S Schueller[11],
P Vergara[12], R Weilenmann[13], J Wilson[14] and A-D Degryse[3]

Central Animal Facility and support functions chart:

purchasing , IT, QA, EHS, biochemistry lab, microbiology lab, tissue processing and histology lab, bioimaging, hygiene services, patent office, legal etc

security. The personnel zone connects to the laboratory

Figure 2.1.3.3 Relational diagram. Typical functional relationships and adjacencies
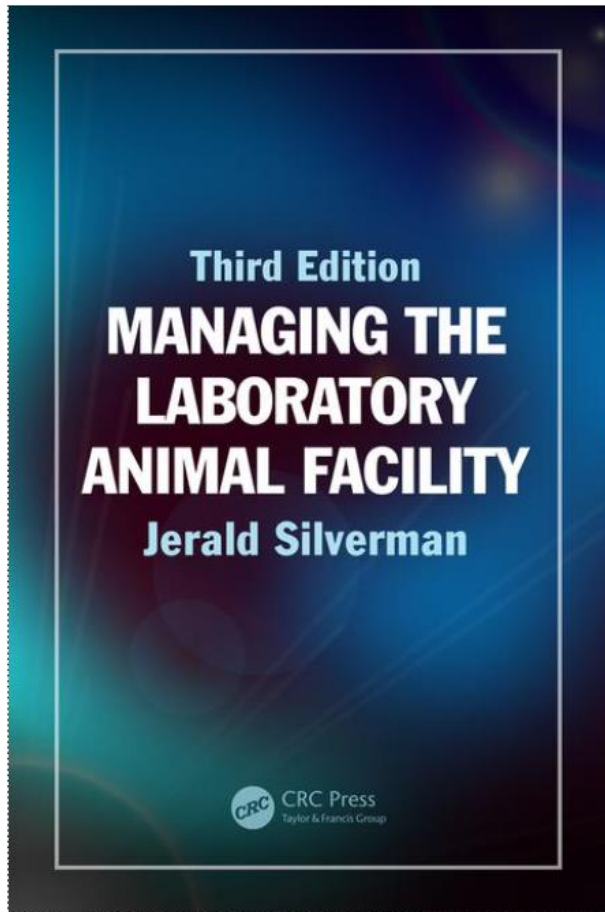ARF = Animal research facility
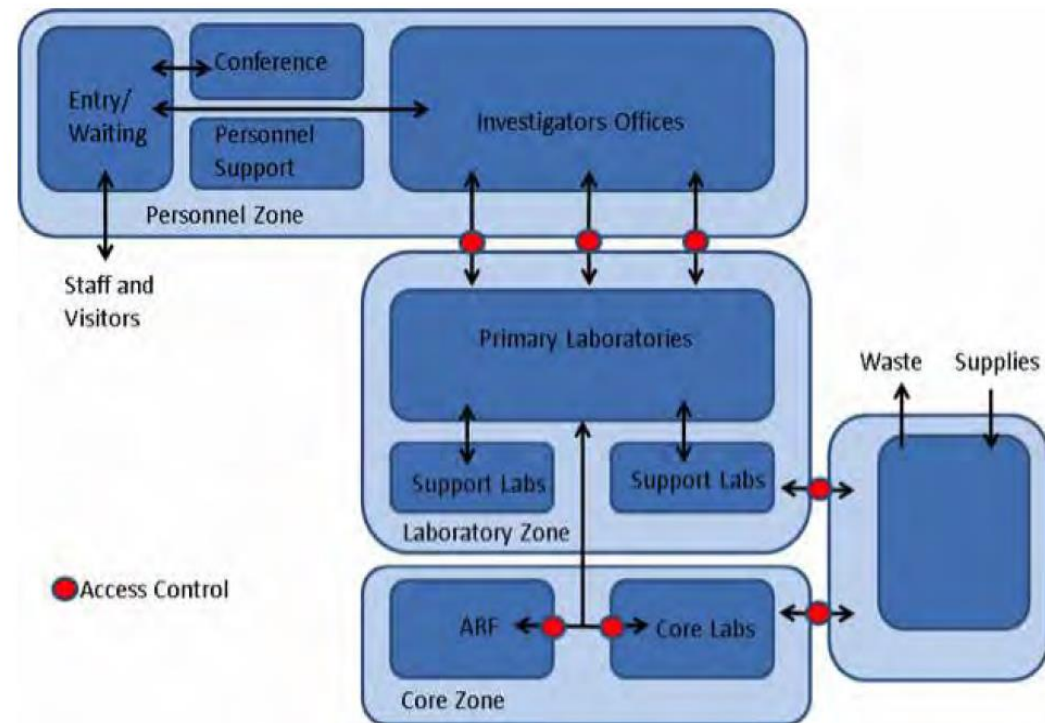
Dual corridor system – division to clean, dirty zones and directed transfer of personnel, animals, equipment and samples

Animal Routes
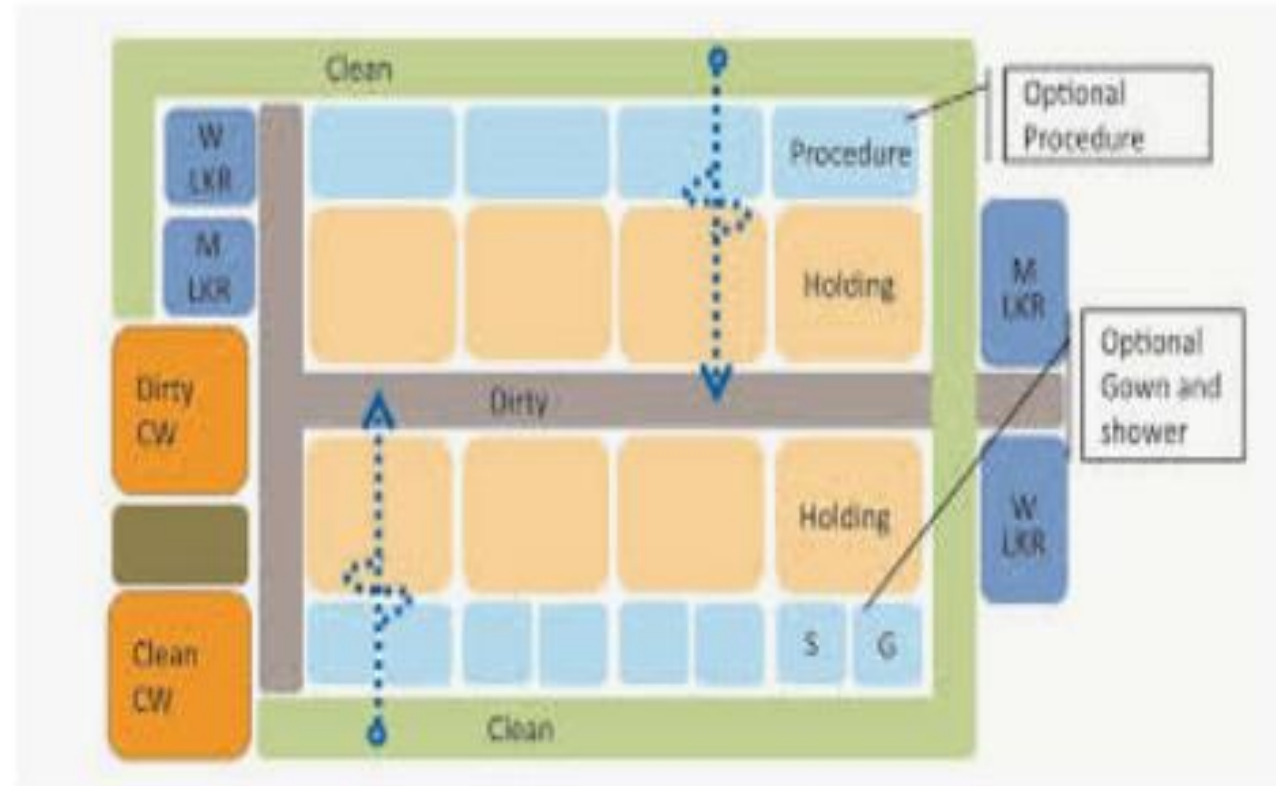
Managing the animal facility: practitioner (e.g. DVM), researcher, manager

Third Edition

MANAGING THE LABORATORY ANIMAL FACILITY

Jerald Silverman

CRC Press
Taylor & Francis Group

Direktor

ostali korisnici

Timaritelji i tehnička asistencija kod izvođenja pokusa

"A pyramid will no longer stand with a top of gold but a base of sand."

Facilitating collaborative animal research: Master Reciprocal Institutional Agreement for Animal Care and Use (2020 publication)

Table 1. *Key elements of the Master Institutional Animal Care and Use Committee (IACUC) Agreement*

Eligibility requirements	• Existence and maintenance of an Animal Welfare Assurance[a] • Existence and maintenance of United States Department of Agriculture (USDA) registration, if working with a USDA-covered species • Maintenance of or commitment to meet the standards required for accreditation from the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC)

Responsibilities	• Ownership: The institution in possession of the animals assumes ownership, unless otherwise agreed upon in advance
	• Congruence between animal protocol and research grant or contract: the institution granted the award is responsible for grant-protocol congruence (may rely on the performance site for the congruency review)
	• Protocol Review: The Performance Site is responsible for ensuring that animal care and use complies with Public Health Service (PHS) Policy, the Animal Welfare Act, the Guide for Care and Use, institutional policies and other applicable laws, statutes, and guidance, as appropriate
	• Rights of institutions: An appropriate institutional representative in a given collaboration may choose to:
	  ○ attend IACUC meeting at institution for protocol review
	  ○ visit the space within which animals are housed or used
	  ○ request minutes of protocol review or semi-annual reports
	  ○ include the site in a post-approval monitoring audit/program

Documentation, Notification, and Reporting	• Performance Site is responsible for compliance with regulatory requirements, including maintaining required documentation; reporting to accrediting, federal, state, and local agencies; and providing this information to the Relying Site upon request (e.g., protocol documents or approvals, significant deficiencies, reports of non-compliance, USDA inspection reports) • Institution receiving grant, contract, or award is responsible for financial regulatory requirements (i.e., reporting non-compliance to funder) • Performance Site must inform relying site(s) of loss or suspension of Office of Laboratory Animal Welfare (OLAW) assurance, USDA registration, or AAALAC accreditation • Each institution must submit its own annual reports to OLAW, USDA, AAALAC, and any other regulatory or oversight organizations • An institution in receipt of a FOIA request must forward that request to the other institution participating in any research protocol that is the subject of or impacted by the request

[a]https://olaw.nih.gov/guidance/topic-index/animal-welfare.htm.

Responsible Biomedical Research:

valuing laboratory animals not as instruments but as patients in an equivalent human medical study

Animal welfare is guarded by **risk mitigation** approaches:

severity categorization and harm/benefit analysis_HBA

(main tools for project i.e. ethical evaluations_PE)

Aurora Brønstad[1], Christian E Newcomer[2], Thierry Decelle[3], Jeffrey I Everitt[4], Javier Guillen[5] and Kathy Laber[6]

Kathy Laber[1], Christian E Newcomer[2], Thierry Decelle[3], Jeffrey I Everitt[4], Javier Guillen[5] and Aurora Brønstad[6]

David Smith[1], David Anderson[2], Anne-Dominique Degryse[3], Carla Bol[4], Ana Criado[5], Alessia Ferrara[6], Nuno Henrique Franco[7], Istvan Gyertyan[8], Jose M Orellana[9], Grete Ostergaard[10], Orsolya Varga[11] and Hanna-Marja Voipio[12]

Reproducibility crisis has lead to increased focus on
factors affecting laboratory animal research outcomes

Table 1 Aspects of an animal care and use program that can affect the quality of preclinical data from animal studies

- Physical plant and environmental conditions (e.g., building material, control of environmental factors, such as temperature, relative humidity, air quality)
- Training (e.g., qualifications, experience, and competence of animal technicians, researchers, veterinarians)
- Oversight (internal, by IACUC/AWB/ethics committee; external, by competent authority; or third-party accreditation, AAALAC International, CCAC)
- Housing (e.g., caging system, space, enrichment, holding room)
- Husbandry (e.g., cleaning and sanitation, food, water, bedding)
- Animal procurement (e.g., source, transport)
- Quarantine and biosecurity practices
- Health monitoring program
- Veterinary interventions
- Surgical program (techniques, asepsis, anesthetic regimens, postsurgical care)
- Pain and distress (e.g., medication, recovery)
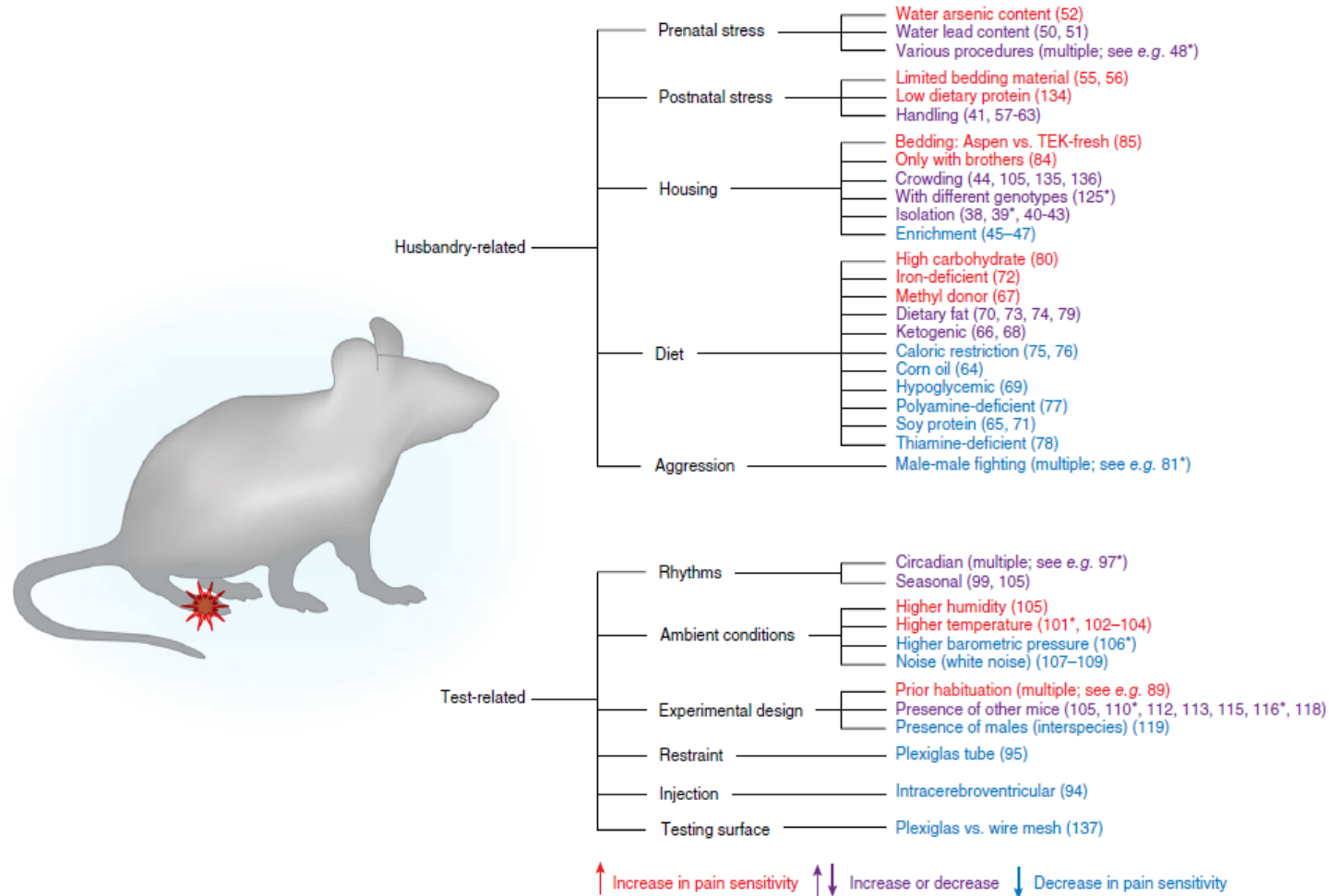- Euthanasia method

FIGURE 1 | Factors significantly affecting pain sensitivity in rodent models and sample references. Only factors that might credibly vary between laboratories are considered. For the factor "Diet", we excluded diabetes, hypertension and obesity models. We also excluded experimental stressors or procedures such as shock, restraint, prolonged maternal separation, or sucrose feeding. Only papers reporting statistically significant effects in either direction are listed. In the case of multiple papers by the same laboratory (indicated by *), only the first to be published is listed.

In EBM_Evidence Based Medicine *clinical evidence* is ranked according to the risk of underlying bias, using the available sources of evidence, from case studies through randomized, controlled clinical trials (RCTs) to clinical trial meta-analyses. The Cochrane Collaboration, which produces systematic reviews of health interventions, now requires authors to use the GRADE approach

To systematically review evidence from animal studies, i.e. the *preclinical evidence*

the Systematic Review Centre for Laboratory Animal Experimentation

(**SYRCLE -** https://www.radboudumc.nl/en/research)

has designed a **SYRCLE risk of bias tool**

based on the Cochrane risk of bias tool (synthesis of evidence_SoE)

NCBI   Resources   How To   Sign in to NCBI

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed ▾ [   ] Search
         Advanced   Help

Format: Abstract ▾   Send to ▾

Full text links

BMC Med Res Methodol. 2014 Mar 26;14:43. doi: 10.1186/1471-2288-14-43.

SYRCLE's risk of bias tool for animal studies.

Hooijmans CR[1], Rovers MM, de Vries RB, Leenaars M, Ritskes-Hoitinga M, Langendam MW.

⊕ Author information

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Quality in Non-GxP Research Environment

During the last decade, the replication and reproducibility crisis in biomedical sciences has exposed severe quality problems in the planning and conduct of research studies in both academia and pharmaceutical industry.

As a result of the reproducibility crisis, which hinges on poor quality of experimental design and resulting data, quality management now has a chance to be introduced in the academic biomedical world.

Pragmatic, risk-based and science driven research quality standards could fit with the discovery activities' scope and requirement of this research activity and ensure data integrity while saving resources.

Risk- and Principle-Based
Quality System Assessment Approach

- In order to ensure data integrity all scientific and business practices should underpin the

  Research Quality System standards

- The fit-for-purpose and tailor-made standards need to contain a set of essential quality system elements that can be applied to all types of research, in a risk-based and flexible manner

3.1   Data Integrity Principles: ALCOA+

ALCOA+

- **A**ttributable (the source of data is identified: who/when created a record and who/when/why changed a record)

- **L**egible (information is clear and readable)

- **C**ontemporaneous (information is recorded at the time of data generation

and/or event observation)

- **O**riginal (source information is available and preserved in its original form)

- **A**ccurate (there are no errors or editing without documented amendments)

+ (additional elements)

- Complete (all data is recorded, including repeat or reanalysis performed)

- Available (data is available and accessible at any time for review or audit and for the lifetime of the record)

- Consistent (harmonized documentation process is constantly applied)

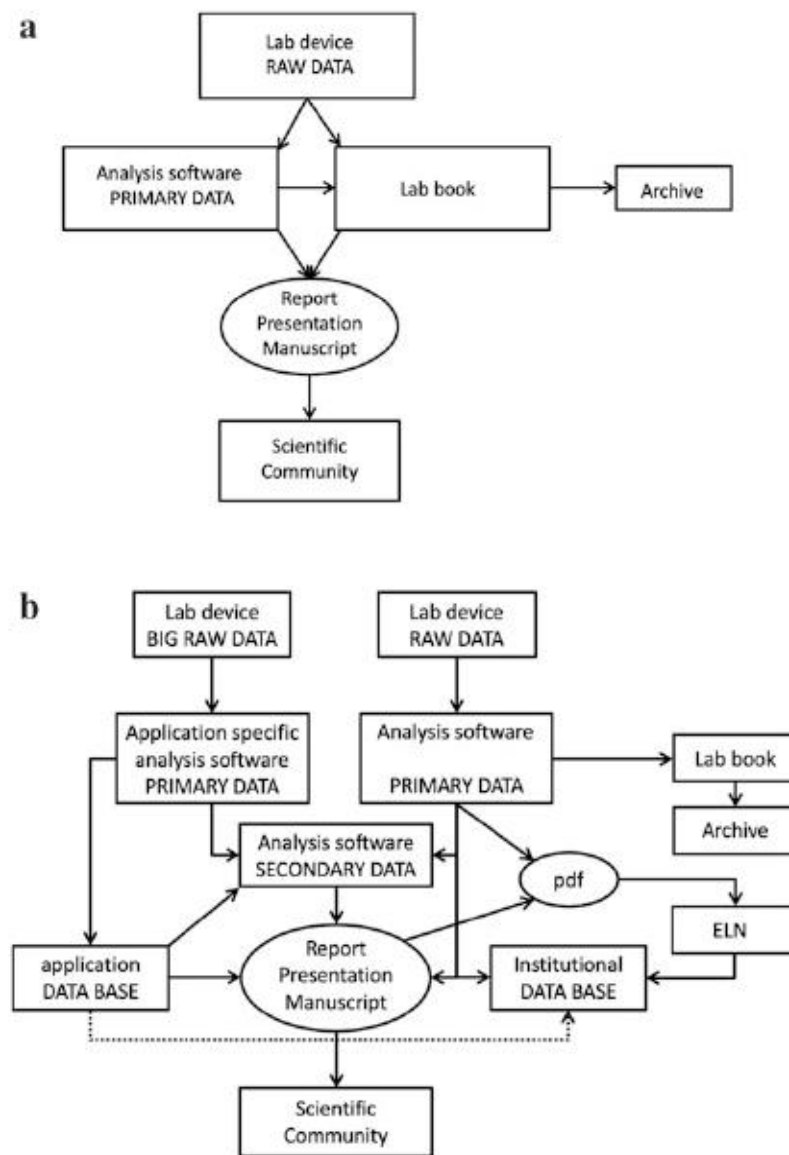- Enduring (data is preserved and retrievable during its entire lifetime)

Fig. 1 (**a**) Traditional data flow: The lab book is an integral part of scientific data flow and serves as a collection of data and procedures. (**b**) An example of a more complex data flow might commonly occur today. Unfortunately, lab books and eLNs are often not used to capture all data flows in the modern laboratory

data and sample traceability (electronic laboratory notebooks_eLNB and LIMS_ laboratory inventory management system)

Identification and definition of research driven processes (e.g.):
- Method and Assay Qualification
- Material, Reagents and Samples Management
- Facility, Equipment and Computerized System Management
- Personnel and Training Records Management

270   B. Gerlach et al.
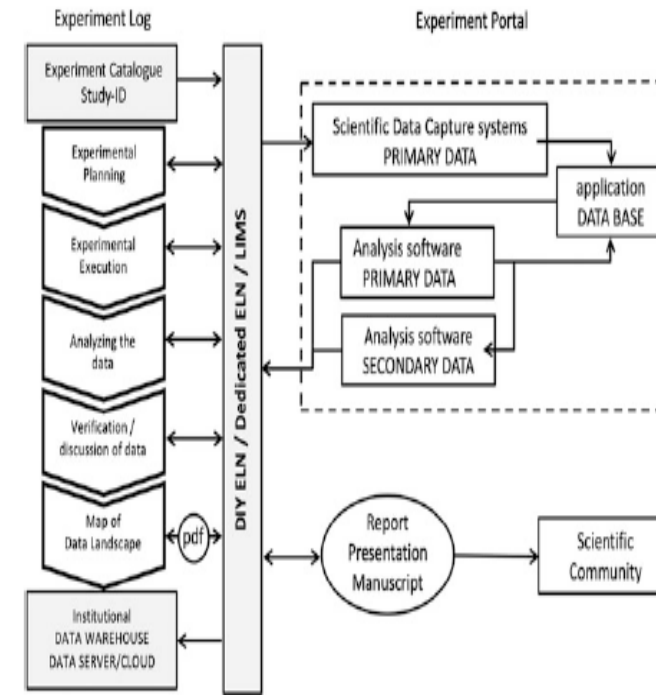
Fig. 2 Workflow for the lab environment with the eLN/LIMS being the central element. Each experimental setup will start with a unique Study-ID entry into the eLN in the experimental catalogue which will be used throughout the whole experiment and allow for tagging during all steps. The eLN will be the hub between the experimental procedure (left) and the data collection and reporting (right). The eLN should collect all different types of data or at least provide the links to the respective storage locations. One of the last steps is the summary of the experiment in the "Map of the Data Landscape" in the form of a PDF file. Next-generation dedicated eLNs could themselves be used to create such a document, thereby providing a document for reporting with the scientific community and storage in the data warehouse

Table 3 General principles to prevent experimental biases in hypothesis testing in vivo studies

Major domains	General principles
Sample size estimation	A power calculation (desired power of at least 0.8, and alpha = 0.05) to estimate the experimental group size should be carried out before any hypothesis testing study using pilot data or those relevant data from the literature. This could be done by using a statistical software. Detail on this can be found in chapter "A Reckless Guide to P-Values: Local Evidence, Global Errors"
Randomisation	There are different methods available to randomly allocate animals to experimental groups such as computer-generated randomisation. One should always consider to use the most robust, appropriate and available method for randomisation. Detail on this can be found in chapter "Blinding and Randomization"
Allocation concealment	Methods should be used to conceal the implementation of the random allocation sequence (e.g. numbered cages) until interventions are assigned, so that the sequence will not be known or predictable in advance by the experimenters involved in allocating animals to the treatment groups
Blinding	Blinding procedures should be carried out, so that the treatment identity should not be disclosed until after the outcome assessments have been finished for all animals and the primary analysis have been completed. In case that one experimenter conducts the whole study, any additional steps should be taken to preserve the blinding. Detail on this can be found in chapter "Blinding and Randomization"
Primary and secondary outcome measures	Experimenters should decide the outcome of great importance regarding the treatment efficacy before any study starts as the primary outcome measure. This is also usually used in the sample size estimation. Primary outcome measure cannot be changed once the study starts and when the results are known. Experimenters should also include secondary outcome measures relating to additional effects of treatments; these may be used for new hypothesis generating
Inclusion/exclusion criteria	Experimenters should set up the exact criteria which will include and exclude animals from their studies. Every animal should be accounted for, except under these criteria. They should be determined appropriately according to the study nature before the studies commence. Once determined, they cannot be changed during the course of investigation

Table 2 General descriptions for the major domains that contribute to experimental biases

Major domains	General descriptions
Sample size estimation	The sample size refers to the number of experimental units (e.g. a single animal, a cage of animals) per group. In hypothesis testing experiments, it should be determined with a power calculation. Studies that are not appropriately powered are unethical, and both underpowered and overpowered studies lead to a waste of animals. The former because they produce unreliable results and the latter because they use more animals than necessary
Randomisation	Refers to the steps to reduce systematic differences between comparison groups. Failure to conduct randomisation leads to selection bias
Allocation concealment	Refers to the practice of concealment of the group or treatment assignment (i.e. the allocation) and its sequence of each experimental unit from the experimenter until the time of assignment. Failure to conceal allocation will lead to selection bias. This should not be confused with randomisation
Blinding	Refers to the practice of preventing the experimenter who administer treatments, take care of the animals, assess the responses and analyse data from knowing the test condition. Failure of appropriate blinding leads to selection, performance and detection biases
Primary and secondary outcome measures	Primary outcome measure refers to the outcome measure of most interest, and it is related to the efficacy of an intervention that has the greatest importance for a given study. Secondary outcome measure refers to the outcome measure that is related to intervention efficacy but with less importance than the primary outcome measure and is used to evaluate additional intervention effects. It is important to declare what intervention effects are in the study protocol
Inclusion/exclusion criteria	Refers to criteria by which animals will be included or excluded in a given study, e.g. due to abnormal baselines or not reaching the required change in thresholds after designed experimental insult

Table 1 Bias definition and bias-reducing methods (Lazic et al. 2018)

Name of bias	Definition of bias	Methods to reduce bias
Selection bias	Refers to the biased allocation of animals to different treatment groups, which could happen at the beginning of an animal study or at a stage where reassigning animals to different treatment groups is needed following an initial surgical procedure or treatment. Selection bias results in systematic differences in baseline characteristics between treatment groups (Higgins et al. 2011)	To avoid systematic differences between animals allocated to different treatment groups, one shall use a valid randomisation method, e.g. a randomisation software or even a simple method such as picking a number from a hat (Baastrup et al. 2010; Huang et al. 2013; Saghaei 2004). Detail for randomisation is covered in chapter "Blinding and Randomization". Note that it is also necessary to conceal the allocation sequence from experimenters who will assign animals to treatment groups until the time of assignment
Performance bias	Related to the systematic differences in the care that is provided between different treatment groups or being exposed to factors other than the treatment that could influence the performance of the animals (Higgins et al. 2011; O'Connor and Sargeant 2014; van der Worp et al. 2010). Performance bias is a result of animals being managed differently due to, e.g. housing conditions, diet, group sizes per cage, location in the animal house, and experimenters who provide the care to animals are not blinded to treatment groups	One can avoid performance bias by improving the study design, e.g. applying the same housing, diet, location conditions to all the animals and by ensuring proper blinding of the experimenters to treatment groups, which keeps the experimenters who perform the experiment, collect data and access outcomes unaware of treatment allocation. Detail for blinding is covered in chapter "Blinding and Randomization"
Detection bias	Defined as the systematic distortion of the results of a study that occurs when the experimenter assessing behavioural outcome measures has the knowledge of treatment assignment to groups (van der Worp et al. 2010). In this circumstance, experimenters measuring the outcomes may introduce differential measurement of the outcomes rather than the treatment itself due to inadvertent expectation	The only way to avoid detection bias is a complete blinding of the experimenters, including those who analyse the data, so that they are not aware which animal(s) belong to which treatment group(s). The protocol should define at what stage the blinding codes will be broken (preferably only after data analysis has been completed). Detail for blinding is covered in chapter "Blinding and Randomization"
Attrition bias	Is the unequal occurrence and handling of deviations from protocol and loss to follow-up between treatment groups (van der Worp et al. 2010). This bias can occur when animals die or are removed from the study due to adverse effects of the treatment or pre-set criteria for	Experimenters should report attrition information for each experimental group and also include outcomes that will not be affected by attrition. It is also advisable to consult a statistician to minimise the impact of attrition bias using some statistical approaches such as intention-to-treat analysis by

ILAR journal vol 55 no 3, 2014_Experimental design and statistics contents (free access archives)

- The Design and Statistical Analysis of Animal Experiments: Introduction
- Refinement of Experimental Design and Conduct in Laboratory Animal Research
- Animal Husbandry and Experimental Design
- Evidence Should Trump Intuition by Preferring Inbred Strains to Outbred Stocks in Preclinical Research
- Critical Appraisal of Studies Using Laboratory Animal Models
- Meta-Analyses of Animal Studies: An Introduction of a Valuable Instrument to Further Improve Healthcare
- The Usefulness of Systematic Reviews of Animal Experiments for the Design of Preclinical and Clinical Studies
- Randomized Block Experimental Designs Can Increase the Power and Reproducibility of Laboratory Animal Experiments
- The Place of Experimental Design and Statistics in the 3Rs
- Making the Most of Clustered Data in Laboratory Animal Research Using Multi-Level Models
- Guidance for description of animal studies in sci publications_Nat Acad Press

in vitro disciplines and relevant standards

Table 1 Examples of minimum information checklists from different disciplines, to ensure the reproducibility and appropriate interpretability of experiments within their domains

Name	Scope/goal	Developer	Link/publication
ENCODE	Experimental guidelines, quality standards, uniform analysis pipeline, software tools, and ontologies for epigenetic experiments	ENCODE consortium	https://www.encodeproject.org/data-standards/ (Sloan et al. 2016)
MIABE	Descriptions of interacting entities: small molecules, therapeutic proteins, peptides, carbohydrates, food additives	EMBL-EBI industry program	http://www.psidev.info/miabe (Orchard et al. 2011)
MIAME	Specification of microarray experiments: raw data, processed data, sample annotation, experimental design, annotation of the array, laboratory and data processing protocols	FGED society	http://fged.org/projects/miame/ (Brazma et al. 2001)
MIAPE	Minimum set of information about a proteomics experiment	Human proteome organization (HUPO) proteomics Standards initiative	http://www.psidev.info/miape (Binz et al. 2008)
MIFlowCyt	Flow cytometry experimental overview, sample description, instrumentation, reagents, and data analysis	International Society for Analytical Cytology (ISAC)	http://flowcyt.sourceforge.net/miflowcyt/ (Lee et al. 2008)
MIMIx	Minimum information guidelines for molecular interaction experiments	HUPO proteomics Standards initiative	http://www.psidev.info/mimix (Orchard et al. 2007)
MIQE	Quantitative PCR assay checklist, including experimental design, sample, nucleic acid extraction, reverse transcription, target information, oligonucleotides, protocol, validation, and data analysis	Group of research-active scientists	http://www.rdml.org/miqe.php (Bustin et al. 2009)
MISFISHIE	Specifications for in situ hybridization and IHC experiments: experimental design, biomaterials and treatments, reporters, staining, imaging data, and image characterization	NIH/NIDDK stem cell genome anatomy projects consortium	http://mged.sourceforge.net/misfishie/ (Deutsch et al. 2008)
STRENDA	Reagents and conditions used for enzyme activity and enzyme inhibition studies	STRENDA consortium	http://www.beilstein-institut.de/en/projects/strenda (Tipton et al. 2014)

IHC immunohistochemistry, *NIH* National Institutes of Health, *NIDDK* National Institute of Diabetes and Digestive and Kidney Diseases, *PCR* polymerase chain reaction

www Laboratory Animal Science and Medicine (LASM)
quality-resources

The use of databases, information centres and guidelines when planning research that may involve animals

AJ Smith[*†] and T Allen[‡]

† Laboratory Animal Unit, Norwegian School of Veterinary Science, Oslo, Norway
‡ Animal Welfare Information Center, US Department of Agriculture, Beltsville, Maryland, USA
* Contact for correspondence and requests for reprints: adrian.smith@veths.no

LASM relevant categories on www

Specialist databases and **3R information centers**

offer a collection of up-to-date LAS specialist guidelines

(the distinction between literature databases and scientific journals is disappearing due to development of free access and open access journals)

EU Commission_ animals used for scientific purposes

https://ec.europa.eu/environment/chemicals/lab_animals/index_en.htm (''guidance documents'' on severity assessment framwork, Project Evaluation and Retrospective Assessment etc)

Norecopa_ Norway

ECVAM_EU Center for Validation of Alternative Methods_alternatives search guide

NC3Rs_UK

FELASA (EU) – Working group reports, recommendations, *Laboratory Animals* official journal

Center for Alternatives to Animal Testing_USA

Canadian Council on Animal Care

ECLAM/ESLAV

AVMA (Association of Veterinary Medical Association_USA)_2020 euthanasia guide

EU wide **national 3R centers**

RSPCA
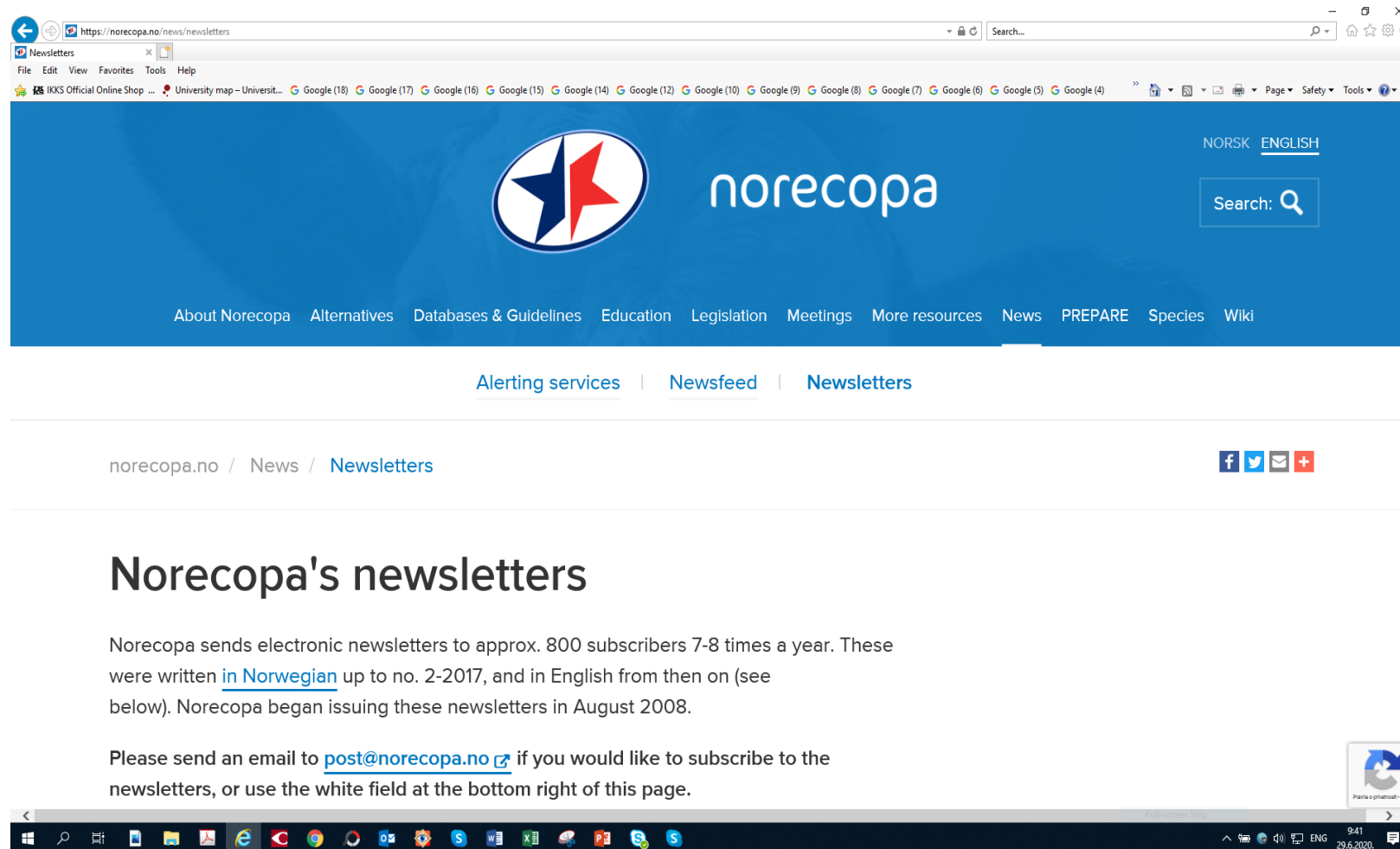
FRAME

ICLAS

Pubmed etc

Norecopa
one-stop-shop for those looking for guidelines and resources within lab animal science and alternatives – subscribe to newsletter for regular updates

European 3R centres

FICAM
Fincopa
Norecopa
Swedish 3R-Centre
SWETOX
Danish 3R-Center
NC3Rs
BB3R
Bf3R
Charité
VZET
3Rs-Centre Utrecht
R2N
IC-3Rs
Walcopa
Tarc force 3R
SET
Czech 3Rs Center
SNP3Rs
ICAR3R
CAAT Europe
EUSAAT
RepRefRed
MUI
HUCOPA
ROCAM
3RCC
Francopa
IPAM
EURL ECVAM
Centro 3R
CMCiB
REMA

Please note that some of these Centres, such as EURL ECVAM, serve more than the country in which they have been placed.

This overview has been compiled by Norecopa. Please report any errors or send suggestions for additions to post@norecopa.no

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Journals (& e-books) as knowledge databases +
(academia & industry publicly available parts of websites)

- *Laboratory Animals* journal
(official journal of FELASA, ESLAV, LAVA etc)
- *Lab animals* (NY)
- *JAALAS (American Association for Laboratory Animal Science) journal*
- *ScandLAS (Scandinavian LAS) journal*
- *JoVE (Journal of Visualized Experiments)*
- *Comparative Medicine* journal
- *ILAR (Institute fore Laboratory Animal Research) journal*
- *ATLA (Alternatives to Laboratory Animals) journal*
- *Open access journals ie PLOS One*
- *PLOS Biology etc*

2020 e-publication

Handbook of Experimental Pharmacology   257

Anton Bespalov
Martin C. Michel
Thomas Steckler   *Editors*

Good Research
Practice in
Non-Clinical
Pharmacology
and Biomedicine

EQIPD

Springer Open

Professional
on-line discussion lists,
professional networks, training services & more

- CompMed_USA

- Voles_UK (Vets in Laboratory Animal Medicine)

- Linkedin

- Research Gate

- Research Animal Training (RAT) –

- www.researcanimaltraining.com

previously flaire training (Flecknell)

(the new norm, brought about by pandemic)

- numerous free webinar series (CR, ESLAV etc)

LASM Specialist Guidelines

Guidelines for preparation, design of animal experiments (**PREPARE**) Part 1

(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.

PREPARE Part 2

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.

PREPARE Part 3

	(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.

ARRIVE guidelines
(checklist for publication of results generated in animal research)

	ITEM	RECOMMENDATION
Title	1	Provide as accurate and concise a description of the content of the article as possible.
Abstract	2	Provide an accurate summary of the background, research objectives, including details of the species or strain of animal used, key methods, principal findings and conclusions of the study.
INTRODUCTION		
Background	3	a. Include sufficient scientific background (including relevant references to previous work) to understand the motivation and context for the study, and explain the experimental approach and rationale.
		b. Explain how and why the animal species and model being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.
Objectives	4	Clearly describe the primary and any secondary objectives of the study, or specific hypotheses being tested.
METHODS		
Ethical statement	5	Indicate the nature of the ethical review permissions, relevant licences (e.g. Animal [Scientific Procedures] Act 1986), and national or institutional guidelines for the care and use of animals, that cover the research.
Study design	6	For each experiment, give brief details of the study design including:
		a. The number of experimental and control groups.
		b. Any steps taken to minimise the effects of subjective bias when allocating animals to treatment (e.g. randomisation procedure) and when assessing results (e.g. if done, describe who was blinded and when).
		c. The experimental unit (e.g. a single animal, group or cage of animals).
		A time-line diagram or flow chart can be useful to illustrate how complex study designs were carried out.
Experimental procedures	7	For each experiment and each experimental group, including controls, provide precise details of all procedures carried out.
		For example: a. How (e.g. drug formulation and dose, site and route of administration, anaesthesia and analgesia used [including monitoring], surgical procedure, method of euthanasia). Provide details of any specialist equipment used, including supplier(s).
		b. When (e.g. time of day).
		c. Where (e.g. home cage, laboratory, water maze).
		d. Why (e.g. rationale for choice of specific anaesthetic, route of administration, drug dose used).
Experimental animals	8	a. Provide details of the animals used, including species, strain, sex, developmental stage (e.g. mean or median age plus age range) and weight (e.g. mean or median weight plus weight range).
		b. Provide further relevant information such as the source of animals, international strain nomenclature, genetic modification status (e.g. knock-out or transgenic), genotype, health/immune status, drug or test naïve, previous procedures, etc.

	ITEM	RECOMMENDATION
Housing and husbandry	9	Provide details of:
		a. Housing (type of facility e.g. specific pathogen free [SPF]; type of cage or housing; bedding material; number of cage companions; tank shape and material etc. for fish).
		b. Husbandry conditions (e.g. breeding programme, light/dark cycle, temperature, quality of water etc for fish, type of food, access to food and water, environmental enrichment).
		c. Welfare-related assessments and interventions that were carried out prior to, during, or after the experiment.
Sample size	10	a. Specify the total number of animals used in each experiment, and the number of animals in each experimental group.
		b. Explain how the number of animals was arrived at. Provide details of any sample size calculation used.
		c. Indicate the number of independent replications of each experiment, if relevant.
Allocating animals to experimental groups	11	a. Give full details of how animals were allocated to experimental groups, including randomisation or matching if done.
		b. Describe the order in which the animals in the different experimental groups were treated and assessed.
Experimental outcomes	12	Clearly define the primary and secondary experimental outcomes assessed (e.g. cell death, molecular markers, behavioural changes).
Statistical methods	13	a. Provide details of the statistical methods used for each analysis.
		b. Specify the unit of analysis for each dataset (e.g. single animal, group of animals, single neuron).
		c. Describe any methods used to assess whether the data met the assumptions of the statistical approach.
RESULTS		
Baseline data	14	For each experimental group, report relevant characteristics and health status of animals (e.g. weight, microbiological status, and drug or test naïve) prior to treatment or testing (this information can often be tabulated).
Numbers analysed	15	a. Report the number of animals in each group included in each analysis. Report absolute numbers (e.g. 10/20, not 50%[2]).
		b. If any animals or data were not included in the analysis, explain why.
Outcomes and estimation	16	Report the results for each analysis carried out, with a measure of precision (e.g. standard error or confidence interval).
Adverse events	17	a. Give details of all important adverse events in each experimental group.
		b. Describe any modifications to the experimental protocols made to reduce adverse events.
DISCUSSION		
Interpretation/ scientific implications	18	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 any potential sources of bias, any limitations of the animal model, and the imprecision associated with the results[2].
		c. Describe any implications of your experimental methods or findings for the replacement, refinement or reduction (the 3Rs) of the use of animals in research.
Generalisability/ translation	19	Comment on whether, and how, the findings of this study are likely to translate to other species or systems, including any relevance to human biology.
Funding	20	List all funding sources (including grant number) and the role of the funder(s) in the study.

ARRIVE

The ARRIVE Guidelines: Animal Research: Reporting of In Vivo Experiments. Originally published in PLOS Biology, June 2010[1]

Guidelines for **facility and equipment sanitation** practices and animals' health monitoring_HM practices

📄 Adoption of Exhaust Air Dust Testing in SPF Rodent Facilities. JAALAS 2020.pdf

📄 CAGE PROCESSING issue 2016.pdf

📄 Comparing Mouse Health Monitoring Between Soiled-bedding Sentinel and Exhaust Air Dust Surveillance Programs. JAALAS 2020.pdf

📄 Transportation of animals NAP 2017.pdf

Working Party Report

Genetic quality assurance and genetic monitoring of laboratory mice and rats: FELASA Working Group Report

Fernando Benavides[1] ⓘ, Thomas Rülicke[2] ⓘ, Jan-Bas Prins[3,4], James Bussell[5], Ferdinando Scavizzi[6], Paolo Cinelli[7], Yann Herault[8,9] and Dirk Wedekind[10]

📄 Biosafety in Biosafety Labs 2009.pdf

📄 Disinfection_Nov_2008.pdf

📄 guide_for_biosafety_competencies 2011.pdf

📄 Influence of olfactory environment on rodents LA 2016.pdf

📄 rodent pathogen contamination of cells and biologics ILAR 2008.pdf

Guidelines for handling animals during experimental procedures: examples of **administration** guidelines

- Dose calculation and stock solution preparation. Journal of Natural Sci Research 2014. pdf.pdf
- Gad SC et al. Tolerable levels of nonclinical vehicles and formulations used in studies by multiple routes and species. Int J Tox 2016.pdf
- JAALAS adm of subst in lab animals 2011.pdf
- JAALAS equipm, vehicle and solute selection for adm od sbst in lab animals   2011.pdf
- Li et Zhao. Developing early formulations. Int J of Pharmaceutics 2007.pdf
- Manual Restraint and Common Compound Administration Routes in Mice and Rats. J Vis Exp 2012..pdf
- Neervannan S. Preclinical Formulations for Discovery and Toxicology_Physicochemical Challenges. Expert Opinion Drug Metab Toxicol 2006.pdf
- NIH US Guidelines for use of parenteral fluids in lab animals 2016.pdf
- Refining procedures for the administration of substances LA 2001.pdf
- Stegemann et al. When poor solubility becomes an issue. EU J of Pharmaceutical Sciences 2007.pdf

Examples of **tissue sampling** guidelines

A Good Practice Guide to the Administration of Substances and Removal of Blood, Including Routes and Volumes

Karl-Heinz Diehl[1], Robin Hull[2], David Morton[3], Rudolf Pfister[4], Yvon Rabemampianina[5], David Smith[6,*], Jean-Marc Vidal[7] and Cor van de Vorstenbosch[8]

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[7]Department of Nonclinical Drug Safety, Boehringer Ingelheim Pharma GmbH & Co KG, Biberach, Germany
[8]Department of Regulatory Toxicology, Syngenta CTL, Alderley Park, Macclesfield, England
[9]Toxicology, Pathology and Veterinary Services Department, Bayer CropScience, Stillwell, KS, USA

Revised guides for organ sampling and trimming in rats and mice – Part 1

A joint publication of the RITA*) and NACAD**) groups

CHRISTINE RUEHL-FEHLERT[1], BIRGIT KITTEL[2], GERD MORAWIETZ[3], PAUL DESLEX[4], CHARLOTTE KEENAN[5], CHARLES R. MAHRT[6], THOMAS NOLTE[7], MERVYN ROBINSON[8], BARRY P. STUART[9], and ULRICH DESCHL[7]

American Veterinary Medical Association _AVMA Guidelines for the Euthanasia of Animals 2020 Edition

Specialist fields guidelines:
surgery, pain research, arthritis research, stroke, cancer, sepsis, microbiome research etc

- A Review of Pain Assessment Methods in Laboratory Rodents. Comp Med 2019.pdf
- A Review of the Effects of Pain and Analgesia on Immune System Function and Inflammation Relevance for Preclinical Studies. Comp Med 2019.pdf
- Andrews et al. Methodologic bias in preclinical pain research_PPRECISE. PAIN 2016.pdf
- Baumans et al. EE for lab mice and rats and variation in exp results. ScandLAS 2010.pdf
- Clinical Management of Pain in Rodents. Comp Med 2019.pdf
- Colby et al. Considerations for infectious disease research studies using animals. Comp Med 2017.pdf
- Defining and Managing Pain in Stroke and Traumatic Brain Injury Research in animam models. JAALAS 2019.pdf
- Guidelines for the welfare and use of animals in cancer research BJC 2010.pdf
- Hawkins P et al 2015. Applying refinement to the use of mice and rats in RA research. Inflammopharmacology.pdf
- Influence of Pain and Analgesia on Cancer Research Studies. Comp Med 2019.pdf
- Influence of Pain and Analgesia on Orthopedic and Wound-healing Models in Rats and Mice. Comp Med 2019. pdf.pdf
- Lilley E et al. Refinement_of_Animal_Models_of_Sepsis_and_Septic_Shock. Shock 2015.pdf
- Mouse Rehab Research Refinement_spinal cord injury. Plos1 Oct 2019.pdf
- Osuchowski et al. Minimum_Quality_Threshold_in_Pre_Clinical_Sepsis. Shock 2018.pdf
- Pain as a Clinical Factor and Experimental Variable in Research Rodents. Comp Med 2019.pdf
- Smith et al. DEPART-Design and execution of protocols for animal research. Osteoarthritis and Cartilage 2017.pdf
- The IMPROVE Guidelines (ischaemia models_procedural refinements of in vivo experiments). JCBFM 2017.pdf
- The Influence of Pain and Analgesia in Rodent Models of Sepsis. Comp Med 2019.pdf
- The Study of Pain in Rats and Mice. Comp Med 2019.pdf

Rectangular Snip

Examples of **good surgical practice** guidelines

📄 Aseptic-surgery-LASA guideline 2017.pdf

📄 Evaluation of 3 Alcohol-based Agents for Presurgical Skin Preparation in Mice. JAALAS 2020.pdf

📄 Guidelines for survival_rodent_surgery-final_NIH 2017.pdf

📄 jove-protocol-2586-principles-of-rodent-surgery-for-the-new-surgeon 2011.pdf

📄 Maximizing the success of bile duct cannulation studies in rats_recommendations for best practices LA 2017.pdf

📄 The effect of periotoneal air exposure on intestinal mucosal barrier. Gastroent Res & Pract 2014.pdf

📄 Training programme to improve aseptic techniques for rodent surgery JAALAS 2006.pdf

Examples of **ethical evaluation** guidelines

📄 Animal welfare and ethics committee deliberations LA journal 2014.pdf

📄 Animpact Report on Pratice of ethical review across EU 2016.pdf

📄 ethical review considerations of virus induced carcinogenesis and oncolytic viral models. ILAR 2016.pdf

📄 Eurobarometer-2016-Animal-Welfare.pdf

📄 GIRCOR ethicalEvaluationGuide4LaboratoryAnimals.pdf

📄 IACUC protocol requirements. ILAR 2018.pdf

📄 Landi M et al. Incorporating ethics and sci into the 3Rs. JAALAS 2015.pdf

📄 LASA ethical review guidance 2010.pdf

1) ANIMAL CARE AND USE Program Description
(''the Guide'')

- Regulations, Policies, and Principles
- Program Management
- Program Management Responsibility
- The Institutional Official
- The Attending Veterinarian
- The Institutional Animal Care and Use Committee
- Collaborations,
- Personnel Management
- Training and Education,
- Occupational Health and Safety of Personnel
- Personnel Security
- Investigating and Reporting Animal Welfare Concerns
- Program Oversight
- The Role of the IACUC
- IACUC Constitution and Function
- Protocol Review
- Special Considerations for IACUC Review
- Postapproval Monitoring
- Disaster Planning and Emergency Preparedness

2) ENVIRONMENT, HOUSING AND MANAGEMENT

- Animals
- Terrestrial Environment
- Microenvironment and Macroenvironment (Secondary Enclosure)
- Temperature and Humidity
- Ventilation and Air Quality
- Illumination
- Noise and Vibration
- Terrestrial Housing
- Microenvironment (Primary Enclosure)
- Environmental Enrichment
- Behavioral and Social ManagementHusbandry
- Population Management

3) VETERINARY CARE

- Animal Procurement and Transportation
- Animal Procurement
- Transportation of Animals,
- Preventive Medicine
- Animal Biosecurity
- Quarantine and Stabilization
- Separation by Health Status and Species
- Surveillance, Diagnosis, Treatment, and Control of Disease
- Clinical Care and Management
- Medical Management

- Emergency Care
- Recordkeeping
- Surgery
- Training
- Presurgical Planning
- Surgical Facilities
- Surgical Procedures
- Aseptic Technique
- Intraoperative Monitoring
- Postoperative Care
- Pain and Distress
- Anesthesia and Analgesia
- Euthanasia

4) PHYSICAL PLANT_PP

- General Considerations
- Location
- Centralization Versus Decentralization
- Functional Areas
- Construction Guidelines
- CorridorS
- Animal Room Doors
- Exterior Windows
- Floors
- Drainage
- Walls and Ceilings
- Heating, Ventilation, and Air Conditioning (HVAC)
- Power and Lighting

PP_continued

- Storage Areas
- Noise Control
- Vibration Control
- Facilities for Sanitizing Materials
- Environmental Monitoring
- Special Facilities
- Surgery
- Barrier Facilities/Conventional/BSL 3
- Imaging
- Whole Body Irradiation
- Hazardous Agent Containment
- Behavioral Studies
- Aquatic Species Housing
- Security and Access Control

Table 1 (continued)

	Publication	Laboratory notebook
• Randomisation method	✓	✓
• Matching for group assignment (name of variable matched)		✓
• Procedures to minimise bias (e.g. litter, cohort, cage, treatment order)		✓
• SOPs available (Y/N)		✓
Experimenter blinding procedures		
• Procedures to keep treatments blind	✓	✓
• Procedures to keep experimenter blind	✓	✓
• Blinding code and decoding timeline		✓
• SOPs available		✓
Training of experimenters		
• Are experimenters trained and certified in each procedure?	✓	✓
• Method of training and certification		✓
• How often is certification renewed?		✓
Sample		
• Sample size	✓	✓
• Power analysis conducted for each measure for each test	✓	✓
Experimental protocols for each test	✓	✓
• Description	✓	✓
• Tests order and rationale	✓	✓
• Duration of habituation to testing room	✓	✓
• SOPs available (Y/N)		✓
Food/water access during experiment (description)	✓	✓
• Ad libitum or restricted access to food and water during experiment	✓	✓
Adverse/noteworthy events during test	✓	✓
Exclusion criteria	✓	✓
Data processing and analysis	✓	✓
• QC methods		✓
• Primary and secondary measures for each test	✓	✓
• Analysis for each measure for each test	✓	✓
• Check to see if data meets statistical test assumptions	✓	✓
• Treatment of outliers	✓	✓
• Experimental units of analysis (animal/cage/litter)	✓	✓
• Notebooks and data storage		✓
Drug	✓	✓
Name of drug used	✓	✓
Source of drug	✓	✓
Drug batch/sample number	✓	✓
Storage prior to preparation	✓	✓
Drug preparation		✓
• Vehicle name and details of preparation	✓	✓

Table 1 (continued)

	Publication	Laboratory notebook
• Doses and rational	✓	✓
• Dose volume	✓	✓
• Route of administration	✓	✓
• Time of administration and pretreatment time	✓	✓
• Drug storage (cold/dark/duration)	✓	✓
Blood sampling time and method (for bioanalysis)		
• Blood sampling method	✓	✓
• Blood sample volume	✓	✓
• Type of collection tube	✓	✓
• Plasma/serum preparation method	✓	✓
• Plasma/serum freezing and storage	✓	✓
Anaesthesia method and monitoring	✓	✓
Euthanasia method and monitoring	✓	✓
Genotyping tissue collection		
• Age at genotyping	✓	✓
• Method of genotyping	✓	✓
• Is genotyping repeated at end of study? (Y/N)	✓	✓
Tail samples kept (Y/N)		✓
Animal ID		
• Method used to ID animals, frequency of checking		✓
(C) *Animal facility*		
Microbial/pathogen status (if specific pathogen-free (SPF) specify pathogens)	✓	✓
Housing		
• Housing room used		✓
• Experimental rooms used		✓
• Species/sex of animals housed in same room		✓
• Caging type	✓	✓
• Controls in place for position of cages? (e.g. light differences, proximity to door)		✓
• Use of ventilated racks	✓	✓
• Number of animals per cage	✓	✓
• Are cages homogeneous for genotype	✓	✓
• Are animals regrouped at any time? If so, at what age?	✓	✓
Enrichment	✓	
• Type of bedding	✓	✓
• Toys in cage? Running wheel?	✓	✓
• Shredded paper?	✓	✓
• Igloos? Other?	✓	✓
Light/dark cycle	✓	
• Time of lights on/off	✓	✓
• Light/dark change with dawn and dusk light gradient? If Y, over what time frame?	✓	✓

Table 1 (continued)

	Publication	Laboratory notebook
Music/sound used. If so, specify details	✓	✓
Humidity	✓	✓
Type of chow	✓	✓
Water (acidified/tap/distilled/autoclaved/filtered/other?)	✓	✓
Air exchange frequency		✓
Handling		
Frequency and duration of handling	✓	✓
Husbandry		
• No. cage changes/week		✓
• No. health checks/week		✓
Health reports from facility		✓
Personal protective equipment, description		✓
(D) *Approvals and authorisation*		
For example, IACUC or AAALAC approval number and date	✓	✓
Ethical approval statement/animal license application	✓	✓
(E) *Equipment*		
Description of equipment used	✓	✓
• Model number	✓	✓
• Vendor	✓	✓
Calibration		
• Method	✓	✓
• Frequency	✓	✓

Adapted from Brunner et al. (2016)

Occupational Health and Safety (Environment Health and Safety EHS):

- Qualitative Mask FIT testing
- Equipment Risk Assessment (compressed gasses, ionizing radiation), training
- Safe handling of biological and chemical agents
- Optimal operation of containment equipment (oprema sa lokalnim odsina pr. mikrobiološki zastitni kabinet tipa II), changing station, dumping station
- Incidents reporting
- Transport of animal by products within EU (prateća dokumentacija za transport životinjskih nus proizvoda koji nisu namjenjeni prehrani) by road and air
- Waste management (waste categories, temporary and permanent storage, safe disposal)
- Waste water handling (collector etc)

Internal QA

- Pisanje SOP-ova, evidencija izmjena, arhiviranje
- Pisanje eksperimentalnih protokola (-II-)
- Pisanje projektnih/istraživačkih protokola
- Pisanje laboratorijskih dnevnika
- Upravljanje projektima
- Upravljanje dokumentacijom
- Upravljanje podacima i uzorcima (data and sample management)
- Postupanje u slučaju elementarnih nepogoda i nesreća (Business Continuity Plan_ BCP, postupanje sa ljudima, opremom i životinjama u slučaju požara, poplave, zemljotresa, pandemije, provale, nestanka struje – UPS, generator etc)
- Plan internih inspekcija i inspekcijski zapisi, zapisi korektivnih mjera (vanjske i unutarnje inspekcije, logs)
- Rad institucijskog etičkog povjerenstva

BCP – fire, earthquake, flood, pandemic, IT hacking, breach of facility threats

📄 AVMA-Guidelines-for-the-Depopulation-of-Animals_2019.pdf

📄 Crisis planning to manage risks posed by animal rights extremists. ILAR 2010.pdf

📄 Disaster Planning and Research Continuity. ILAR 2018.pdf

📄 Disaster Planning for Animals in Hazardous Agent Containment Units. ILAR 2018.pdf

Information Technology IT

- animal facility access control
- user account and pswrd mngmt
- back up and restore policy
- anti virus and software update procedures
- IT disaster recovery plan etc

Q&A
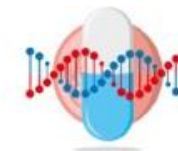
Organizacijska reforma:

definiranje razina odgovornosti i zadataka

Radionica/Workshop

Hvala na pažnji!