Czech Centre for Phenogenomics (CCP)

Policy on the Ethical, Reproducible and Responsible Animal Research

The CCP 5R Framework

1. Preamble and Scope

The Czech Centre for Phenogenomics (CCP) of the Institute of Molecular Genetics of the Czech Academy of Sciences (IMG) is a national large research infrastructure of the Czech Republic and a full member of INFRAFRONTIER and the International Mouse Phenotyping Consortium (IMPC). As a publicly funded facility conducting phenotypic, genetic, and preclinical research involving laboratory animals, CCP operates under obligations that are legal, ethical, scientific, and societal in nature.

This Policy sets out CCP's commitments and governance framework for the care and use of animals in research. It applies to all staff, students, visiting researchers, and collaborating partners who use CCP facilities or services involving live animals. It supersedes any informal guidance previously issued and shall be reviewed no less than every two years or following a significant change in legislation, organisational structure, or scientific scope.

2. Regulatory and Ethical Basis

CCP's animal research activities are conducted in full compliance with:

- **EU Directive 2010/63/EU** on the protection of animals used for scientific purposes, transposed into Czech law (Act No. 246/1992 Coll. of the Czech National Council of 15 April 1992, on the protection of animals against cruelty, as amended);
- Authorisations issued by the relevant Czech national competent authority (Ministry of Agriculture);
- Ethical approvals granted by the CCP Institutional Animal Care and Use Committee (IACUC) of the IMG and Resort Professional Commission of the CAS for Approval of Projects of Experiments on Animals;
- Standards established by **INFRAFRONTIER[1], EMMA[2],** and **IMPC[3]** for harmonised phenotyping and data quality;
- The **ARRIVE 2.0 guidelines[4]** for reporting of *in vivo* animal studies;
- The **NC3Rs Institutional Framework for the 3Rs** and associated self-assessment guidance;
- The **European Charter for Access to Research Infrastructures** (EC, 2024) regarding equitable, open, and responsible access.

[1] INFRAFRONTIER quality principles in systemic phenotyping, Doi: 10.1007/s00335-021-09892-2, The INFRAFRONTIER Quality Management Framework, https://www.infrafrontier.eu/about-us/quality-management/

[2] International Mouse Phenotyping Resource of Standardised Screens, https://www.mousephenotype.org/impress/index

[3] QUALITY PRINCIPLES IN EMMA ARCHIVING AND DISTRIBUTION, https://www.infrafrontier.eu/wp-content/uploads/2025-07-31_EMMA-QualityPrinciples_V02_final.pdf

[4] ARRIVE 2.0 Guidelines, https://arriveguidelines.org/arrive-guidelines

No animal procedure may commence at CCP without: (a) a valid institutional licence; (b) project-level ethical approval; (c) personal certification of all personnel performing, supervising, or caring for animals; and (d) confirmation that the 5Rs have been systematically considered in study design.

3. The CCP 5R Framework — Principles and Commitments

CCP adopts an extended ***five-principle framework*** that builds on the internationally established 3Rs (Russell & Burch, 1959) by adding two further dimensions, the **Reproducibility** and **Responsibility**, that are essential for modern translational research and publicly accountable infrastructure. Together, the 5Rs form a mutually reinforcing system: weaknesses in any one principle undermine the others.

3.1 Replacement

Principle: Avoid or replace the use of live animals wherever a scientifically valid alternative exists.

Rationale: Replacement should be considered at the earliest stage of study design. The development and validation of alternative methods is a scientific endeavour in its own right, not merely a regulatory compliance exercise.

CCP Commitments:

- Maintain an active programme to develop, validate, and disseminate non-animal and *ex vivo* alternatives, including organoid models, iPSC-derived cell systems, precision-cut tissue slices, and *in silico* / computational modelling approaches.
- Provide study design consultancy that explicitly evaluates whether alternatives can address the scientific question, in whole or in part, prior to any animal project being approved.
- Track and report annually the proportion of projects in which validated alternatives replaced or reduced planned animal use.
- Ensure that all staff are trained in the identification and application of replacement methods relevant to their scientific domain.

3.2 Reduction

"Reduction is not about doing less science. It is about designing better science, so that every animal used contributes to a result that matters."

Principle: Use the minimum number of animals necessary to achieve scientifically valid and statistically robust results. Experiments must be designed for reproducibility from the outset. This is the highest priority in ensuring that results can be translated into medical, pharmaceutical, and clinical applications.

Rationale: Animal research is a privilege that carries scientific and ethical responsibility in equal measure. Every animal that does not contribute meaningfully to a valid scientific outcome represents a missed opportunity both for the science and for the welfare commitment that underpins responsible research. ***Reduction therefore demands rigorous study design, not simply fewer animals per protocol.***

CCP Commitments:

- Require a formal a priori power analysis or equivalent statistical and /or scientific justification for all animal projects as a condition of ethical approval. Support will be provided by the CCP Biostatistics and Bioinformatics Unit.

- Promote systematic sharing of biological samples (tissues, cells, biobanked material) across concurrent projects to extract maximum data from each animal.
- Leverage CCP's membership in IMPC and INFRAFRONTIER to pool phenotyping data across centres, thereby reducing per-partner animal numbers while increasing statistical power.
- Maintain a tissue and colony sharing register accessible to all users.
- Discourage colony over-production through proactive breeding management, cryopreservation services (EMMA-archived strains), and timely rederivation from frozen stock.
- Reporting annual animal use figures transparently.

3.3 Refinement

Principle: Continuously improve all aspects of animal housing, husbandry, experimental design, and procedural technique to minimise pain, suffering, distress, and maximize results and data for each experimental approach *in vivo*.

Rationale: Refinement is an ongoing process, not a threshold to be reached once. It encompasses every interaction between personnel and animals and requires a culture of continuous improvement, not merely compliance with minimum standards.

CCP Commitments:

- Maintain SPF (Specific Pathogen Free) barrier housing with individually ventilated caging (IVC), environmental enrichment as standard, and species-specific social housing as the default.
- Apply non-invasive monitoring technologies wherever possible, including telemetric measurement of cardiovascular, metabolic, and neurological parameters to reduce the burden of repeated handling and blood sampling.
- Establish humane endpoints for all severity classifications, reviewed and updated at each project renewal.
- Ensure all personnel working with animals hold current competency certification appropriate to their role (in accordance with Directive 2010/63/EU, Article 23) and receive refresher training no less than every three years.
- Appoint a Named Animal Care and Welfare Officer (NACWO) and Named Veterinary Surgeon (NVS) with sufficient protected time to fulfil their oversight responsibilities.
- Conduct regular adverse event reviews and apply root cause analysis to prevent recurrence.

3.4 Reproducibility

Principle: Ensure that all animal research conducted at CCP produces data that are reliable, transferable, and scientifically valid, enabling translation to medical, pharmaceutical, and industrial applications.

Rationale: Reproducibility is the bridge between animal experimentation and real-world impact. A study that is ethically conducted but produces irreproducible results wastes both animal lives and public resources and actively impedes translation to clinical or commercial application. The reproducibility crisis in biomedical research (estimated to affect 50–70% of preclinical studies) is in large part a study design and reporting problem, not a fraud problem. CCP is uniquely positioned to set and demonstrate a higher standard.

CCP Commitments:

- Apply internationally harmonised Standard Operating Procedures (SOPs) across whole CCP, aligned with IMPC and IMPReSS 2.0 protocols, and make SOPs publicly accessible: CCPs SOPs in IMPC (IMPReSS): *https://www.mousephenotype.org/impress/PipelineInfo?id=44*

- Operate Good Laboratory Practice (GLP)-compliant workflows and extend GLP-compliant quality management principles to research services whenever possible.
- Require pre-registration of study designs (research question, key design features, primary endpoints, and statistical analysis plan) and use the CCP Informatics App before experimental work commences; develop and maintain a registry for animal experiments.
- Mandate compliance with ARRIVE 2.0 guidelines for all publications arising from work conducted at CCP facilities and provide author support to ensure this.
- Deposit all primary phenotyping data in open access repositories (IMPC, or equivalent) within 12 months of data collection, in accordance with FAIR data principles (Findable, Accessible, Interoperable, Reusable); develop CCP database.
- Implement inter-laboratory quality control comparisons with INFRAFRONTIER, IMPC, or other partner centres to detect and correct systematic measurement drift.
- Maintain a Quality Management System (QMS) including document control, internal audits, and corrective action protocols.
- Provide users with access to experimental design and biostatistics consultation at the project planning stage.

3.5 Responsibility

Principle: Exercise the full range of obligations (legal, societal, environmental, and institutional), that attach to a publicly funded national research infrastructure working with animals.

Rationale: Modern research infrastructure must maintain a "social licence to operate": the ongoing trust of the public, patients, policymakers, funders, and the scientific community that justifies the continued conduct of animal research. This licence is not permanent; it must be actively maintained through transparency, accountability, environmental stewardship, and genuine engagement. Responsibility also encompasses obligations to CCP's own staff and to the equitable treatment of all user communities.

CCP Commitments:

Transparency and Public Reporting:

- Publish non-technical summaries of all active project licences in Czech and English, accessible on the CCP website.
- Respond constructively to Freedom of Information requests and proactively engage with regulators during inspections.

Environmental Sustainability:

- Conduct a biennial environmental sustainability audit of CCP facility operations, covering energy consumption, water use, waste generation, and carbon footprint, and publish the results.
- Set progressive reduction targets for environmental impact and report progress annually.
- Prioritise environmentally responsible procurement of animal feed, bedding, and consumables.

Public Engagement and Communication:

- Actively communicate the value, conduct, and oversight of animal research to the public and media, in accordance with the principles of the Concordat on Openness on Animal Research[5].

[5] https://concordatopenness.org.uk/about-the-concordat-on-openness/

- Engage with patient advocacy groups, rare disease communities, and the general public through structured outreach activities (open days, school visits, media engagement).
- Provide accessible online content explaining what animal research is conducted at CCP, why it is conducted, and how it is regulated.

Training and Culture:

- Foster a culture in which animal welfare concerns can be raised without fear of professional repercussions, including a confidential reporting mechanism.
- Require all researchers using CCP services to complete a mandatory orientation covering the 5Rs, ethical approval processes, and data quality expectations.
- Offer and promote external 3Rs training courses and symposia to all staff and users.
- Appoint 5R Champions from among scientific and animal care staff to promote the framework within their teams.

Equitable Access:

- Provide access to CCP services under published, transparent terms that support equitable access for academic groups, SMEs, and international partners.
- Offer study design and 5R consultation as a standard component of all service quotations.
- Apply a merit-based access review for externally funded projects to ensure scientific quality and 5R compliance whenever possible.

4. Governance and Accountability

4.1 Centre and Institutional Oversight

The CCP Director holds responsibility for compliance with this Policy. Day-to-day oversight is delegated to the ***Officer for Animal Welfare and Ethics (OAWE),*** who reports to the CCP director and internal Scientific Advisory Board on an annual basis.

4.2 5R Working Group

A standing 5R Working Group, reporting to the CCP director, internal Scientific Advisory Board and institutional AICUC (“odborná komise UMG pro zajišťování dobrých životních podmínek pokusných zvířat”), is responsible for monitoring progress against the indicators defined in Section 3, coordinating the annual 5R Report, managing the 5R Champions network, and proposing updates to this Policy. The Working Group meets twice a year and includes representatives from each CCP module.

4.3 User Responsibilities

All users of CCP animal facilities and services (including visiting researchers, students, and academic and industry partners) accept the obligations of this Policy as a condition of access. Users are required to:

- Comply with all relevant legislation, ethical approvals, and CCP SOPs;
- Report any concern about animal welfare, study integrity, or data quality to ***OAWE*** without delay;
- Comply with ARRIVE 2.0 reporting standards in all publications arising from CCP-conducted work;
- Acknowledge CCP in all publications and provide CCP with copies of resulting publications.

5. Training Requirements

Role	Required Training	Frequency
All CCP staff	5R Framework orientation	On induction; refresher every 3 years
All animal users (internal)	EU-recognised personal licence (Category B/C/D as applicable)	Maintained continuously
Project Licence Holders	Experimental design and biostatistics	Before first project; refresher every 3 years
Animal care staff	Species-specific husbandry and welfare assessment	Annual
Supervisory staff	5R Framework awareness and ethical review	Before appointment

CCP will maintain a training register for all personnel, auditable by the competent authority.

6. Document Control and Review

This Policy will be reviewed:

- Every two years from the date of approval;
- Following any significant change in applicable legislation;
- Following a major adverse welfare event or regulatory finding;
- At the request of the CCP Director.

All revisions require approval by the CCP Director and discussion in the internal Advisory Board before taking effect. Superseded versions will be archived and accessible on request.

7. Related Documents

- CCP Standard Operating Procedures (SOPs) all phenotyping units (held on Quality Management System) - see quality framework publications:
  - ***A quality framework for cryopreserved rodent disease models: INFRAFRONTIER quality principles in EMMA archiving and distribution. Mamm Genome. 2025 Dec 10;37(1):10. doi: 10.1007/s00335-025-10174-4.***
  - ***Improving laboratory animal genetic reporting: LAG-R guidelines. Nat Commun. 2024 Jul 2;15(1):5574. doi: 10.1038/s41467-024-49439-y.***
  - ***INFRAFRONTIER quality principles in systemic phenotyping. Mamm Genome. 2022 Mar;33(1):120-122. doi: 10.1007/s00335-021-09892-2. Epub 2021 Jul 30.***
  - ***INFRAFRONTIER: mouse model resources for modelling human diseases. Mamm Genome. 2023 Sep;34(3):408-417. doi: 10.1007/s00335-023-10010-7. Epub 2023 Jul 19.***
- IMPC Data Release and Phenotyping SOP Compendium
- ARRIVE 2.0 Guidelines (NC3Rs, 2020)
- EU Directive 2010/63/EU and Czech transposing legislation

8. Contact

For questions about this Policy, ethical review procedures, or the 5R Framework:

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Document Reference: CCP-POL-2026-001
Version: 1.1
Effective Date: 2026-01-07
Review Date: --
Approved by: Radislav Sedlacek, the CCP Director
Document Owner: Officer for Animal Welfare and Ethics, CCP

This Policy is approved by the CCP Director and is publicly available on the CCP website. It reflects CCP's commitment to conducting animal research that is ethically sound, scientifically excellent, and socially responsible.