INFRAFRONTIER QUALITY PRINCIPLES IN EMMA ARCHIVING AND DISTRIBUTION

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1. INTRODUCTION

INFRAFRONTIER is a pan-European Research Infrastructure that offers a range of research services related to disease models to the scientific community, including archiving and distribution of mouse and rat strains through the European Mouse Mutant Archive (EMMA) consortium. While the INFRAFRONTIER vision is to contribute to human health by advancing disease prevention and therapies through appropriate models, the European Mouse Mutant Archive is a unified repository for maintaining biomedically relevant mutant rodent strains, which are made available to the scientific community.

EMMA's motivation for all quality measures applied is to preserve and distribute mutant strains of high quality, building on material and mutant description received from the provider, carefully validating and applying the genotyping protocols provided to identify carriers of the specific mutation(s), performing health screening, as well as extensive data curation. Strains are only accepted into EMMA after scientific and technical evaluation and the level of quality control is described in order confirmations and summarized at https://www.infrafrontier.eu/emma/strain-distribution/quality-control/.

Reflecting this the INFRAFRONTIER Quality Principles at hand were developed by the INFRAFRONTIER Quality Management (QM) Network Group and representatives of the different EMMA nodes as a set of internally agreed key quality standards for EMMA Archiving and Distribution activities. Thus, they provide the framework for EMMA's operational procedures which are defined in the internal EMMA Operational Handbook and obligatory to be observed by all nodes. At the same time, the Principles recognize that local circumstances at the different European national nodes may differ and that different schemes may be chosen for the application of these standards.

Each principle is divided in four sections, i.e. context, requirements, recommendations, and relevant references. The context sections are meant to "set the scene". They provide information about the underlying background of the principles, e.g. specific conditions and circumstances which need to be considered. Thus, they point out the relevance of the specific principles for INFRAFRONTIER. Key are the requirement sections which list mandatory points, i.e. procedures which need to be implemented at the nodes to fulfil the respective principles. In addition, the recommendation section of each principle proposes further procedures and measures which will improve adherence to the principles but are not mandatory. Finally, the references list regulations,

publications, and links to webpages, which are referred to in the other sections or provide useful information. A complete list of references and URLs can be found in the Annex.

2. Overview of the EMMA Quality Principles

(1) We strictly comply to national and European legislation on the protection of animals used for scientific purposes

(2) We promote and apply the ethical and animal welfare principles - 3Rs (Replacement, Reduction, Refinement)

(3) We follow good scientific practices

(4) We apply Standard Operating Procedures

(5) We ensure that our procedures are carried out by competent and trained personnel

(6) We put emphasis on keeping timely, direct, professional, and transparent interaction with our users

(7) We ensure that submitted strains are evaluated by external experts in a transparent and open manner

(8) We strive to make our services available for all researchers while respecting intellectual property

(9) We provide models with curated and FAIR data (findable, accessible, interoperable, reusable)

(10) We maintain and extend the mechanisms (working groups, training, exchange of experience) to constantly share information and improve our quality

3. DETAILS (CONTEXT – REQUIREMENTS – RECOMMENDATIONS - REFERENCES)

(1) We strictly comply to national and European legislation on the protection of animals used for scientific purposes

Context:

- In its function as an archive for biomedically relevant rodent models all EMMA partners must comply with the Directive 2010/63/EU and its amendments including its national transpositions (or as applicable the respective UK legislations) and other relevant Animal Health and Welfare policies and recommendations
- To support EMMA's commitment to establish highest possible animal welfare standards:
    - We created an INFRAFRONTIER/EMMA Animal Welfare Expert (AWEX) group
    - We established a Scientific Advisory Board which consists of independent individuals who are experts in the field of modern mammalian genetics and animal welfare

Requirements:

- All activities needed for the archiving and distribution at the EMMA partners are compliant with EU and national laws and covered by respective licences
- Compliance includes, but is not limited to:

  All activities involving animal use are assessed through a local ethical review procedure by competent authorities, both internal and external, to
    - validate applied procedures
    - review animal care and accommodation standards
    - evaluate the "harm/benefit" balance of applied procedures

  Staff members are advised and kept up to date on animal welfare regulations and the 3Rs

  It is ensured that all personnel involved in animal use have been adequately trained

Recommendations:

- As far as possible, it is confirmed that recipients of live animals, embryos or gametes work under the guidance of an institutional ethical review body / process
- Follow the recommendations of the European Expert Groups (e.g. NC3Rs, EC):

https://environment.ec.europa.eu/topics/chemicals/animals-science_en, https://www.nc3rs.org.uk

References:

- DIRECTIVE 2010/63/EU (EU Parliament and Council 2010) and its applicable national transitions
- Commission Implementing Decision (EU) 2020/569 (European Commission 2020)
- The Animal (Scientific Procedures) Act 1986 Amendment Regulations 2012 (UK Statutory Instruments 2012)
- EC website (European Commission 2025), animals in science: https://environment.ec.europa.eu/topics/chemicals/animals-science_en
- NC3Rs website (NC3Rs 2025): https://www.nc3rs.org.uk/
- Framework for the genetically altered animals under Directive 2010/63/EU on the protection of animals used for scientific purposes (European Commission, Directorate-General for Environment 2022)
- Directive 2010/63/EU on protection of animals used for scientific purposes – Severity assessment framework (European Commission, Directorate-General for Environment 2018)
- Guide for the Care and Use of Laboratory Animals: Eighth Edition (National Research Council 2011)
- INFRAFRONTIER website (INFRAFRONTIER 2025): https://www.infrafrontier.eu/about-us/animal-welfare-and-ethics/

(2) We promote and apply the ethical and animal welfare principles - 3Rs (Replacement, Reduction, Refinement)

Context:

- According to the current EMA (European Medicines Agency) guideline the 3Rs are:
  - **Replacement:** "testing approaches that avoid or replace the use of live animals in an experiment where they would have otherwise been used. Replacement could include the use of established animal and human cell lines, or cells and tissues or mathematical and computer models or physicochemical methods." In addition, according to NC3Rs (NC3Rs 2025 , https://www.nc3rs.org.uk/who-we-are/3rs) partial replacement is the use of animals that, based on current scientific understanding, are not considered capable of experiencing suffering, such as Drosophila and nematode worms.

- **Reduction**: "approaches that minimise the number of animals used per experiment or study, either by enabling researchers to obtain comparable levels of information from fewer animals, or to obtain more information from the same number of animals, thereby avoiding further animal use. Examples include improved experimental design and statistical analysis, combination of studies, international harmonisation of testing requirements (e.g. (V)ICH) to avoid duplicate testing and the use of technologies, such as imaging, to enable longitudinal studies in the same animals."
- **Refinement**: "approaches that minimise the pain, suffering, distress, or lasting harm that may be experienced by the animals. Refinement applies to all aspects of animal use, from the housing and husbandry used to the scientific procedures performed on them. An example of refinement is the use of appropriate anaesthetics and analgesics."

- Genetically modified rodent models for human diseases play a major role in basic and biomedical research to understand molecular mechanisms of human disorders and for the development of new therapies. As a repository providing cryopreservation of valuable mouse and rat strains, by the nature of its operation, EMMA is promoting sustainability and reproducibility in science and directly contributing to a significant reduction in the number of experimental animals being used. All resources available through the EMMA network are easily accessible and made visible via the INFRAFRONTIER website. Moreover, EMMA strongly promotes the shipment of frozen material to minimise the welfare issues associated with the movement of live animals
- Replacement, Reduction, and Refinement of animal use (the 3Rs principle) provides EMMA with a solid framework to continually rethink and optimise its experimental approaches in archiving, quality assays and distribution

Requirements:

- According to Directive 2010/63/EU on the protection of animals used for scientific purposes, Article 4:
  - "...ensure that, wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure."
  - "... ensure that the number of animals used in projects is reduced to a minimum without compromising the objectives of the project."
  - "...ensure refinement of breeding, accommodation and care, and of methods used in procedures, eliminating or reducing to the minimum any possible pain, suffering, distress or lasting harm to the animals."
- REDUCTION in EMMA:

    - Reduce duplicate testing by ensuring visibility and accessibility to strains and data
    - Careful colony size management to ensure that supply matches demand
    - Whenever possible, use of surplus animals for other scientific purposes
    - Regular reviews to ensure that those strains which are not being requested or are only used sporadically are not (longer) maintained as livestock
    - Implementation of cryopreservation protocols that minimise the number of animals
    - Genotyping of blastocysts instead of live mice as Quality Control (QC) step
- REFINEMENT in EMMA:
    - Reduce, eliminate, or relieve discomfort, pain, distress or anxiety experienced by animals, e.g.
        - Harmful effects associated with gene modifications are minimised by maintaining heterozygous strains
        - Improved procedures (vasectomy, in vitro fertilisation (IVF), embryo transfer) in accordance with veterinary advice
        - Use of least invasive methods (e.g. for embryo transfer or to provide an adequate sample for genotyping)
        - Use appropriate anaesthetics and analgesics in accordance with veterinary advice and regulatory requirements
        - Perform appropriate and humane killing methods
    - Improve the conditions of transport, breeding, and accommodation
        - All EMMA personnel involved are well-trained and highly competent to provide the necessary level of husbandry and care to minimise any suffering in all the animal procedures undertaken from birth to death
        - Enrichment of the accommodation environment
        - High health status of the mouse/rat colonies
        - Promote shipping of samples (frozen or refrigerated sperm / embryos or tissue) rather than live animals
        - Live animal transportations comply with the LASA (Laboratory Animals Science Association) and IATA (International Air Transport Association) regulations
    - All welfare information associated with a particular strain and any specialist care required is provided via public databases
- REPLACEMENT in EMMA

- The EMMA consortium has been established to cryopreserve and distribute genetically altered rodents on behalf of the scientific community. There are no alternatives to the use of live animals for this activity
- Available phenotypic information about potentially embryonical lethal genes may guide users to alternative models

- Verify compliance to 3Rs requirements in ethical review processes

Recommendations:

- Constant technology development for the implementation of the 3Rs in experimental procedures
- Exchange of knowledge of 3R related developments between INFRAFRONTIER / EMMA partners
- Aim to publish all relevant research data to avoid unnecessary repetition of animal studies
- Live animal transportation is done only when no other possibility available

References:

- Directive 2010/63/EU (EU Parliament and Council, 2010) and its applicable national transitions
- Directive 2010/63/EU on protection of animals used for scientific purposes – Animal welfare bodies and national committees (European Commission, Directorate-General for Environment, 2018)
- Guideline on regulatory acceptance of 3Rs testing approaches EMA/CHMP/CVMP/JEG-3Rs/450091/2012 (EMA, 2016)
- IATA website (IATA, 2025): https://www.iata.org
- INFRAFRONTIER website (INFRAFRONTIER, 2025), Animal Welfare: https://www.infrafrontier.eu/about-us/animal-welfare-and-ethics/
- LASA website (LASA, 2025): https://www.lasa.co.uk
- LASA. Guidance on the transport of laboratory animals (Swallow et al 2005)
- NC3Rs website (NC3Rs, 2025), 3Rs: https://www.nc3rs.org.uk/who-we-are/3rs
- EURL ECVAM dataset on alternative methods to animal experimentation (DB-ALM) (European Commission, Joint Research Centre (JRC), 2019)
- VICH website (VICH, 2025): https://www.vichsec.org

(3) We follow good scientific practices

Context:

- Ensuring data and research integrity, within an EMMA facility and across EMMA nodes, i.e.
    - reliability (of procedures etc.),
    - honesty (in reporting etc.),
    - respect (for animals, colleagues, etc.),
    - accountability (of offered non-profit research service, etc)

Requirements:

- Ensure controlled housing conditions / environment according to EU and national regulations (Directive 2010/63/EU and applicable national transitions)
- Monitor and report health status of the mouse and rat strains in line with FELASA (Federation of European Laboratory Animal Science Associations) recommendations
- Follow animal welfare considerations and regulations and apply the 3Rs principles
- Ethical evaluation of all activities involving animal treatment
- Define the most appropriate cryopreservation, rederivation, and breeding protocols
- Use validated methods / protocols, that means Standard Operating Procedures (SOPs) which have been proven to robustly deliver reproducible results (e.g. ensured by repeated execution, re- / cross-check in case of modifications; see also Principle (4))
- Ensure the standard quality control level as summarized on the INFRAFRONTIER webpage. Each strain submitted to EMMA goes through a genetic control process which involves genotyping imported strains for the mutation(s) of interest as part of the archiving and/or distribution process
- Ensure traceability and transparency of applied procedures. Record data and metadata and provide it (upon request). Refer to ARRIVE (Animal Research: Reporting of In Vivo Experiments) and PREPARE (Planning Research and Experimental Procedures on Animals: Recommendations for Excellence) guidelines
- Provide the user / requester with all the relevant information concerning the mouse / rat strains (strain descriptions, archiving / recovery / genotyping protocols and distribution options, as applicable)
- Observe common general EMMA procedures as outlined in the internal EMMA Operational Handbook
- Ensure clearly communicated roles and responsibilities (within the EMMA facilities, between EMMA nodes and users (archiving and distribution))
- Disseminate knowledge (e.g. EMMA partner institutions offer cryopreservation training courses)

Recommendations:

- Apply tests / procedures validated previously across EMMA nodes, e.g. by strain comparison or pharmacological validation, whenever possible
- Consider phenotyping of EMMA strains where the development was phenotype driven and the mutation is not known
- Exchange among EMMA nodes about relevant parameters (e.g. fertilisation rate) and, as applicable, reference strains to validate new SOPs and harmonise tests / procedures
- Implement best practice throughout the operation
- Design processes to minimise the impact on animal welfare, e.g. promote the exchange of embryos and germplasm and minimise the shipment of live animals whenever possible
- Discourage the exchange of stocks between researchers and encourage researchers to return to the archive to minimise the impact of genetic drift and accidental cross-contamination of strains
- Use statistical analysis, where appropriate (see also Principle (4))

References:

- ARRIVE guidelines (Kilkenny et al, 2010; Percie du Sert, 2020a; Percie du Sert, 2020b) ; https://arriveguidelines.org/
- Directive 2010/63/EU (EU Parliament and Council, 2010) and its applicable national transitions
- FELASA website (FELASA, 2025): https://felasa.eu
- NC3Rs website (NC3Rs, 2025), 3Rs: https://www.nc3rs.org.uk/who-we-are/3rs
- NIH website (NIH, 2025), Rigor and Reproducibility: https://grants.nih.gov/policy/reproducibility/index.htm
- PREPARE guidelines (Smith et al, 2018)
- Handbook: Quality practices in basic biomedical research (WHO TDR, 2006)
- The European Code of Conduct for Research Integrity (ALLEA, 2017)
- INFRAFRONTIER website (INFRAFRONTIER, 2025),
    - EMMA: https://www.infrafrontier.eu/emma/
    - EMMA Cryopreservation Protocols: https://www.infrafrontier.eu/emma/cryopreservation-protocols/
    - EMMA standard quality control: https://www.infrafrontier.eu/emma/strain-distribution/quality-control/

(4) We apply Standard Operating Procedures

Context:

- Key principle: Ensure consistent quality, reach repeatability, reproducibility and robustness of applied methods, ensure transparency, preserve knowledge and ease knowledge transfer
- Standard Operating Procedures (SOPs)
    - provide specifications and step-by-step instructions for (complex) routine operations / activities
    - regulate how specific EMMA procedures are physically carried out including data management and organisation
- All EMMA partners use validated and state-of-the art protocols for relevant procedures such as embryo and spermatozoa freezing techniques, in vitro fertilisation procedures, embryo transfers, and genotyping of submitted / requested strains. Thawing and IVF protocols are provided to users ordering frozen embryos or spermatozoa

Requirements:

- Implement and maintain node-specific SOPs for EMMA procedures (archiving, quality control (QC), distribution) and related activities like animal welfare, training of staff
- Define
    - responsibilities, operational methods, parameters and metadata to be measured, recorded, evaluated and reported, including QC steps
    - controlled equipment, service and calibration intervals, and resources / consumables
    - as applicable, appropriate statistical analysis to ensure work is robust and reproducible
- Install periodic SOP reviews that also consider any recent technical innovations
- Exercise document version control within the node to ensure the most up to date SOPs are used (disseminate latest SOP version, withdraw outdated versions).
- Observe defined common EMMA operational procedures as laid down in the internal EMMA Operational Handbook

Recommendations:

- Evaluate repeatability and reproducibility of methods / protocols
- Devise a system of independent internal audits to ensure SOPs are being followed and are fit for purpose. Define the purpose of the audit, e.g. if only certain elements of the SOP are being specifically audited (procedure, staff competency, suitability of the document)

References:

- Handbook: Quality practices in basic biomedical research (WHO TDR, 2006). Chapter 4.3.2 Standard operating procedures
- INFRAFRONTIER website (INFRAFRONTIER, 2025):
    - EMMA Cryopreservation Protocols: https://www.infrafrontier.eu/emma/cryopreservation-protocols/
    - EMMA standard quality control: https://www.infrafrontier.eu/emma/strain-distribution/quality-control/

(5) We ensure that our procedures are carried out by competent and trained personnel

Context:

- Each EMMA node activity requires adequately qualified and trained personnel as training is essential in order to ensure that procedures are carried out in a reproducible way and generate consistent quality
- On-site training is complemented by EMMA / INFRAFRONTIER training workshops and exchange of experience in regular meetings of dedicated working groups
- Compliance to regulatory training requirements (e.g. European Directive 2010/63 and its transposition in each country) is ensured
- Recording of personnel competencies is managed by the different EMMA nodes

Requirements:

- Definition of job requirements and responsibilities for each level of personnel
- Ensure that all staff receive the required training / qualifications and maintain the competence and skill level to complete techniques to a satisfactory standard. Record these professional development / training qualifications and competency proofs, e.g. in up-to-date training plans / records / competency logs, to keep track of individual training and competence status and demand
- Continual training should be available in the form of regular training, carried out by competent and experienced trainers
- All personnel who handle animals must be suitably qualified and undergo training to maintain the required competency level and/or to update their skills and their awareness of the 3Rs
- Compliance with local regulations must be ensured (e.g. experimental activities with animals may only be carried out by personnel with the respective personal licences)

Recommendations:

- Training activities should be regularly and independently reviewed / audited
- As far as possible, provide more than one person with the competencies to carry out a given procedure in order to limit operator effects
- Staff members must undergo refresher training if they have not done a technique for a period of time (e.g. 6 months), for example to ensure correct animal handling and to mitigate potential personnel safety risks
- Training of applicable complementary guidelines (e.g. PREPARE, FAIR, ARRIVE, ALLEA)
- Knowledge transfer by regular exchange of experience e.g. via meetings and dedicated training workshops across EMMA nodes

References:

- AAALAC Accreditation Program (AAALAC, 2025)
- ARRIVE guidelines (Kilkenny et al, 2010; Percie du Sert, 2020a; Percie du Sert, 2020b)
- Directive 2010/63/EU (EU Parliament and Council, 2010) and its applicable national transitions
- GO FAIR website (Go FAIR, 2025), FAIR Principles: https://www.go-fair.org/fair-principles/
- ISO 9001 Quality Management Systems (ISO, 2015)
- The European Code of Conduct for Research Integrity (ALLEA, 2017)
- PREPARE guidelines (Smith et al, 2018)
- Handbook: Quality practices in basic biomedical research (WHO TDR, 2006). Chapter 4.1.2 Personnel and training
- INFRAFRONTIER website (INFRAFRONTIER, 2025), trainings: https://www.infrafrontier.eu/training-events/

(6) We put emphasis on keeping timely, direct, professional, and transparent interaction with our users

Context:

- Users of EMMA archiving and distribution service are scientists either looking to deposit mutant rodent strains in a repository or obtaining them via EMMA
- A scientific user support group serves as a central contact point while service specifics are clarified in direct communication between user and individual centre archiving / distributing the respective strain
- Protocols for relevant lab procedures are shared with users, e.g. via the INFRAFRONTIER website, and likewise training courses are offered

- User feedback is collected on a regular basis and monitored centrally
- EMMA records 'key performance indicators' (KPIs) which track various elements of the service processes and can be used for benchmarking

Requirements:

- Ensure that personal and sensitive data is treated according to the appropriate regulations (e.g. General Data Protection Regulation (GDPR))
- Communicate clearly what the user can expect from the EMMA service requested, especially with regard to any limitations associated with their inquiry, e.g. by disclaimers on the website, but also in direct communication with the user
- Respond in a timely manner to user enquiries (e.g. answer to emails usually within 2 days), both on central user support and on EMMA node side
- Make it clear to the users which input is needed from their end in order to avoid delays in service provision
- Inform the user as soon as possible in a professional/factual manner if there are going to be any unexpected delays/issues when dealing with their request. Provide support as and when necessary
- Regularly request user feedback by the standard (prefilled) user feedback forms for both users who have deposited strains and users who have ordered mutant strains. Respond to complaints promptly and honestly

Recommendations:

- Regular review and exchange (at least yearly) among EMMA partners on performance indicators, user feedback, and, as necessary, actions to be taken
- EMMA nodes share recent protocols and training offers for users with the central user support for publishing via the INFRAFRONTIER website

References:

- Regulation (EU) 2016/679 (General Data Protection Regulation) (EU Parliament and Council, 2016)
- GDPR.EU website (GDPR.EU, 2025): https://gdpr.eu
- INFRAFRONTIER website (INFRAFRONTIER, 2025):
  - Sharing of EMMA protocols: https://www.infrafrontier.eu/emma/cryopreservation-protocols/
  - INFRAFRONTIER data privacy statement: https://www.infrafrontier.eu/data-privacy/

(7) We ensure that submitted strains are evaluated by external experts in a transparent and open manner

Context:

- EMMA's ambition is to provide access to valuable mutant rodent strains with significance for current and future biomedical research. To ensure this, strains submitted to EMMA undergo an evaluation process, which involves an external scientific evaluation and is based on the information provided during submission. Major evaluation criteria are: sound scientific methods, evidence of heritability, identifiable genotype, and stabilised phenotype
- The external evaluation committee is composed of experts in the field of rodent genetics
- For strains from certain projects (e.g. EC funded) that have their own selection process, the EMMA evaluation step is omitted. Examples are EUCOMM/KOMP (including allele converted strains being deposited to EMMA), International Mouse Phenotyping Consortium (IMPC) and INFRAFRONTIER2020
- While the Evaluation Committee is the priority setting body regarding deposition of mutant strains into EMMA, final decision whether it archives an accepted strain or not lies with the EMMA nodes (e.g. based on balance between archiving costs and expected distribution income and technical feasibility). If rejected by an EMMA node, the scientific user support team will try to find an alternative archiving node
- A scientific user support group serves as a central contact and coordination point for all evaluation activities, including communication and follow up with the submitter

Requirements:

- Keep barrier to application low and thus provision of sound strain information by offering accessible, well-structured and user-friendly online form
- At EMMA scientific user support level, make sure that a certain minimum of information is available prior to the external evaluation or otherwise ask the submitter to provide it.
- Assure transparency of the evaluation results by having the external evaluators fill in an evaluation form with different questions agreed among all of them, the different EMMA nodes, and the INFRAFRONTIER data curators. Make evaluation criteria accessible to users via the INFRAFRONTIER webpage
- If a strain has been rejected by one evaluator, the scientific user support team shall involve two additional evaluators and only if both recommend accepting, the strain can be accepted

- Cultivate open and transparent communication with submitters including information about the evaluation process, openness about reasons for rejection or concerns, and giving the opportunity to provide additional information if not sufficient in the first place
- Generally, ensure that personal and sensitive data submitted is treated according to the appropriate regulations (e.g. General Data Protection Regulation (GDPR)). All members of the INFRAFRONTIER external evaluation committee (evaluators) must have signed a 'Confirmation of Non-Disclosure of Information' document

Recommendations:

- If a submission has been rejected, offer the submitter to come back with additional information. The evaluation can be reopened in this case
- If the distribution of strain via EMMA has been rejected, allow the possibility that EMMA partners can offer a fee-for-service archiving

References:

- Regulation (EU) 2016/679 (General Data Protection Regulation) (EU Parliament and Council, 2016)
- GDPR.EU website (GDPR.EU, 2025): https://gdpr.eu
- INFRAFRONTIER website (INFRAFRONTIER, 2025):
  - General information on EMMA: https://www.infrafrontier.eu/emma/
  - EMMA evaluation criteria: https://www.infrafrontier.eu/emma/cryopreservation/
  - Members of the INFRAFRONTIER external evaluation committee: https://www.infrafrontier.eu/external-evaluation-committee/
- Further operational specification of evaluation process as described in the EMMA Operational Handbook (internal INFRAFRONTIER / EMMA document, current version)

(8) We strive to make our services available for all researchers while respecting intellectual property

Context:

- EMMA services are generally available to all scientists working at academic research institutions. Access for industry is possible if the depositor and requester agree on terms of transfer
- When depositing a strain at EMMA, the intellectual property and the ownership of material remain with the provider. INFRAFRONTIER/EMMA merely has a coordinating

and brokering role. Any existing Material Transfer Agreement (MTA) will remain in full force and effect

Requirements:

- As far as possible EMMA partners provide unrestricted access to the EMMA services offered via the INFRAFRONTIER webpage (local import / export limitations might apply)
- It is ensured centrally that the EMMA legally binding general conditions are accepted when submitting or requesting a mutant strain (e.g. via obligatory check boxes on the respective forms)
- The provider is obliged to either be the sole allele/strain owner or to have permission from all owners to deposit the strain into the EMMA repository. Confirmation during the online submission process is mandatory
- If the submitter asks for delayed release of material and data, e.g. as the deposited strain has not been published, it is safeguarded centrally that this grace period is respected as granted (e.g. through corresponding status notes in the database)
- When applicable, the EMMA nodes only exchange animals, germplasm or embryos when an MTA between requester and owner has been fully executed (or a licence agreement in case of commercial requests)

Recommendations:

- Consider recommendations of the ALLEA working group 'Intellectual Property Rights' and UBMTA templates

References:

- INFRAFRONTIER website (INFRAFRONTIER, 2025), EMMA general conditions: https://www.infrafrontier.eu/emma/legal-questions/
- ALLEA Permanent Working Group Intellectual Property Rights (ALLEA, 2025): https://allea.org/intellectual-property-rights/
- UBMTA (Uniform Biological Material Transfer Agreement) (autm, 2025): https://autm.net/surveys-and-tools/agreements/material-transfer-agreements/mta-toolkit/uniform-biological-material-transfer-agreement

Operational specification of submission process as set in the EMMA Operational Handbook (internal INFRAFRONTIER / EMMA document, current version)

(9) We provide models with curated and FAIR data (findable, accessible, interoperable, reusable)

Context:

- Each strain submitted to EMMA undergoes manual (community-submitted strains) or programmatic (IKMC-IMPC etc. automatically submitted strain) data curation including strain nomenclature and background(s) / gene(s) / mutation type(s) / allele(s) / transgene(s) etc. attribute assignments, according to the rules and guidelines of the International Committee on Standardized Genetic Nomenclature for Mice.
- FAIR data and services aim to improve reproducibility of biomedical research, to drive new scientific discoveries and to enable any researcher in Europe and across the world to access and use them. The meaning of FAIR according to go-fair.org is:
    - **Findable:** Metadata and data should be easy to find for both humans and computers.
    - **Accessible:** Once the user finds the required data, she/he/they need to know how they can be accessed, possibly including authentication and authorisation.
    - **Interoperable:** The data usually needs to be integrated with other data. In addition, the data needs to interoperate with applications or workflows for analysis, storage, and processing.
    - **Reusable:** Goal is to optimise the reuse of data. To achieve this, metadata and data should be well-described so that they can be replicated and/or combined in different settings
- INFRAFRONTIER-EMMA has been reviewed, selected, and listed as a FAIR-compliant ("FAIR-fied") resource by the reference FAIRsharing International Consortium
- INFRAFRONTIER is a partner/member of the European Open Science Cloud. Through heterogeneous projects INFRAFRONTIER integrates with the other European Biological and Medical Research Infrastructures to create an open, collaborative digital space for life science and to ensure the FAIR availability of Europe's life science data.

Requirements:

- Check, correct and update each submitted strain's data records by standardised curation procedures (refer to internal EMMA Operational Handbook), including
    - Compliance to the approved format for the nomenclature of mouse mutant strains: strain background(s)-mutant locus(i)/allele(s) and/or expressed transgene(s)/holding site(s) code(s)
    - Correct assignment of symbols or abbreviations for each of the above nomenclature components, as approved upon Mouse Genome Informatics (MGI) review

    - Correct identification of each approved locus, allele or transgene symbol, as well as approved strain name by a unique MGI ID value, which is inserted in the INFRAFRONTIER-DB
- Ensure that personnel involved in data curation processes are aware of and understand the meaning and application of FAIR principles
- Maintain procedures and Information Technology (IT) services to ensure compliance of EMMA data to the FAIR principles (see https://www.go-fair.org/fair-principles/):
    - **Findable:** Each mutant strain receives a unique and persistent identifier and is described with as much detail as available from the provider. Related resources are also provided reusing their unique identification number. Genes, alleles and all relevant information related to a mutant mouse strain are described using common nomenclatures and ontologies. All terms/identifiers are searchable via the EMMA public strain search
    - **Accessible:** The data is accessible via the INFRAFRONTIER webpage. In addition, essential information about all EMMA strains is made accessible through interfaces of specific alternative platforms (e.g. IMSR)
    - **Interoperable:** Mutant mouse strains names follow the official strain nomenclature provided by the MGI. Mouse strain data is integrated with external resources (e.g. IMPC phenotype data and MGI disease annotations) using ontologies and controlled vocabularies
    - **Reusable**: Utilisation of well-established standards from the community (e.g. Mammalian Phenotype ontology and Disease ontology)**.** Data provenance is provided, e.g. by documentation of the experimental production of the strains
- Ensure data protection requirements are fulfilled and all users of the EMMA repository service agree to the EMMA data privacy policy. Except for relevant information on producer (and additional owner, if applicable) name and affiliation, as well as strain information, no personal / sensitive data must be displayed on the public EMMA strain search

Recommendations:

- Increase accessibility to EMMA data via integration with other platforms (e.g. EJP RD, EOSC-Life)
- Consider recording additional data for new strains according to relevant guidelines for genetic reporting (e.g. LAG-R)

References:

- FAIR Principles:
    - GO FAIR website (GO FAIR, 2025): https://www.go-fair.org/fair-principles/

    - The FAIR Guiding Principles for scientific data management and stewardship (Wilkinson M et al, 2016)
- FAIR metrics: A design framework and exemplar metrics for FAIRness (Wilkinson M et al, 2018)
- EMMA on FAIRsharing.org (FAIRsharing.org, 2025): https://doi.org/10.25504/FAIRsharing.g2fjt2
- EMMA—mouse mutant resources for the international scientific community (Wilkinson P et al, 2010): https://doi.org/10.1093/nar/gkp799
- INFRAFRONTIER-providing mutant mouse resources as research tools for the international scientific community (INFRAFRONTIER Consortium, 2015): https://doi.org/10.1093/nar/gku1193
- INFRAFRONTIER: mouse model resources for modelling human diseases (Ali Khan A et al, 2023): https://doi.org/10.1007/s00335-023-10010-7
- EJP RD website (EJP RD, 2025): https://www.ejprarediseases.org/
- EOSC-Life website: https://www.eosc-life.eu (EOSC-Life 2025)
- IMPC website (IMPC, 2025):
    - IKMC: https://www.mousephenotype.org/about-impc/about-ikmc/
    - Phenotype data: https://www.mousephenotype.org/understand/data-collections/
- International Mouse Strain Resource website (IMSR, 2025): https://www.findmice.org/repository
- MGI website (MGI, 2025):
    - Rules and guidelines established by the International Committee on Standardized Genetic Nomenclature for Mice: https://www.informatics.jax.org/mgihome/nomen/index.shtml
    - Mammalian Phenotype Ontology: https://www.informatics.jax.org/vocab/mp_ontology
- Regulation (EU) 2016/679 (General Data Protection Regulation) (EU Parliament and Council, 2016)
- INFRAFRONTIER website (INFRAFRONTIER, 2025):
    - INFRAFRONTIER data privacy statement: https://www.infrafrontier.eu/data-privacy/
    - EMMA nomenclature service and integrated resources: https://www.infrafrontier.eu/emma/cryopreservation/nomenclature-service-and-integrated-resources/
- Further operational specifications for data curation as described in the EMMA Operational Handbook (internal INFRAFRONTIER / EMMA document, current version)

(10) We maintain and extend the mechanisms (working groups, training, exchange of experience) to constantly share information and improve our quality

Context:

- To facilitate continuous improvement, we apply the **PDCA (Plan-Do-Check-Act)** concept. PDCA is an iterative, four-stage approach for continually improving processes, products or services, and for resolving problems. It provides a simple and effective approach for solving problems and managing change and enables users to develop hypotheses about what needs to be changed, to test these hypotheses in a continuous feedback loop, and to gain valuable learning and knowledge.

  The PDCA cycle consists of four components:

  Plan – Identify the problem / the improvement opportunity, collect relevant data / information, understand the problem's root causes / the improvement options, and prioritise which ones to test

  Do – Develop a potential solution / improvement approach, decide upon a measurement to gauge its effectiveness, and test it

  Check – Confirm the results e.g. through pre- and post- data comparison, study the result, measure effectiveness, and determine whether or not the problem was resolved / the intended improvement was achieved

  Act – Document the results. If the solution / improvement approach was successful, implement it and inform others about process changes. If not successful, tackle the next possible cause / decide whether another improvement option should be tested and repeat the PDCA cycle again
- Customer feedback is regularly asked for by common EMMA feedback forms for both users who have deposited strains and users who have ordered mouse/rat strains. User feedback and other service performance indicators such as number of archived strains are recorded centrally and monitored on node and Scientific User Support level
- To continually improve the processes at INFRAFRONTIER / EMMA, we perform inter-centre exchange of experience through dedicated working groups, e.g. a QM EMMAgroup for exchange on EMMA operational and quality topics like the EMMA Quality Standards

Requirements:

- Commitment to quality policy and principles from all personnel at all levels
- Implement procedures to monitor local processes against the INFRAFRONTIER quality principles and the quality objectives set by the EMMA node, e.g.

- Collection and evaluation of user feedback. As applicable, definition and analysis of corresponding measures
- Process monitoring, e.g. by reviewing of EMMA common performance monitoring data and other (local) key performance indicators as applicable
- Error management
- Invest in training of quality awareness

- The outcome of these quality procedures are corrective and/or preventive actions and action plans to support continuous improvement

Recommendations:

- Participate in the INFRAFRONTIER/EMMA working groups (e.g. QM EMMA group)
- Consider a common set of principles to ensure quality, such as Quality Management System (QMS) requirements stated in e.g. ISO 9001, GLP, AAALAC and aim for certification/accreditation
- Consider establishing a Quality Manual / top-level document that describes an organisation's QMS
- Consider risk and opportunity management (e.g. according to ISO 9001)
- Report any deviations to procedures etc., e.g. in a non-conformity log, and assess them as appropriate. Evaluate the (long term) impact of changes introduced to correct for deviations
- Conduct regular quality reviews (e.g. annually)
- Consider assigning an independent internal reviewer to assess processes and recommend improvements and / or external reviews or site visits by domain experts
- Consult e.g. OECD reference framework for impact assessment of Research Infrastructures

References:

- AAALAC Accreditation Program (AAALAC, 2025)
- ISO 9001 Quality Management Systems (ISO, 2015)
- Principles on Good Laboratory Practice (GLP) (OECD, 1998)
- Reference framework for assessing the impact of research infrastructures (OECD, 2019)
- QM framework in BMS RIs (BBMRI-ERIC et al, 2017)

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5. HISTORY OF CHANGES

Version	Date	Chapter	Changes
V01	06 Dec 2023	–	–
V02	31 Jul 2025	QP1 (context), 1st point	Editorial change: Clarification that adherence to Directive 2010/63/EU includes any amendments
-/-	-/-	QP 7 (evaluation), requirements, 2nd bullet point	Procedural change: Evaluators agreed that CRISPR-specific criteria of availability of peer-reviewed phenotyping information has proven unnecessary - deleted.
-/-	-/-	QP 7 (evaluation), requirements, 4th bullet point	Procedural change: When a strain has been rejected by one evaluator, two instead of previously one additional evaluator will be consulted. Strain acceptance requires confirmation by both.
-/-	-/-	QP9 (FAIR data), requirements, 3rd bullet point	Editorial change: Clarification that IT services are involved in maintaining FAIR compliance
-/-	-/-	QP9 (FAIR data), recommend., 2nd bullet point	New point: Introduction of new LAG_R guideline and general recommendation for recording of additional strain data acc. to relevant reporting guidelines
-/-	-/-	QP10 (improve), context, 3rd bullet point + recommend., 1st bullet point	Minor procedural update: reference to Technical Working Group removed as group is inactive
-/-	-/-	Entire Document	Editorial changes: *animal usage* replaced by *animal use* in line with wording in EU Directive. Harmonisation of formatting for individual terms (e.g. Directive instead DIRECTIVE), harmonisation of punctuation, reference styles, spelling corrections
-/-	-/-	References	Verification of website links