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A quality framework for cryopreserved rodent disease models: INFRAFRONTIER quality principles in EMMA archiving and distribution

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Abstract
Ensuring the quality and reproducibility of biological resources is essential for advancing biomedical research and upholding animal welfare standards. The European Mouse Mutant Archive (EMMA), part of the INFRAFRONTIER research infrastructure, plays a key role in this effort by cryopreserving scientifically validated mutant mouse and rat strains and making them accessible to the global scientific community. To further enhance its processes and promote transparency, INFRAFRONTIER/EMMA has developed a set of ten Quality Principles specifically tailored to the unique requirements of cryopreserved rodent mutant strains. These principles guide EMMA's workflows by providing a structured yet flexible quality framework across its distributed nodes. They encompass both general standards—such as adherence to the 3Rs (Replace, Reduce, Refine), staff competence, and continuous improvement—and more specific areas including scientific evaluation, data curation, and intellectual property rights. Each principle is presented with contextual background, defined requirements, practical recommendations, and key references. This initiative aims to strengthen the reliability, ethical integrity, and reproducibility of preclinical research resources.

Introduction

The European Mouse Mutant Archive (EMMA) is a cornerstone of INFRAFRONTIER, the European Research Infrastructure for modelling human diseases (Wilkinson et al. 2010; INFRAFRONTIER Consortium 2015; Raess et al. 2016; Ali Khan et al. 2023). As Europe's largest nonprofit, centralized yet distributed rodent strain repository, EMMA is dedicated to the long-term cryopreservation and worldwide distribution of genetically altered rodent strains—primarily mice, but also rats (www.infrafrontier.eu). These animal models remain an essential component of understanding human disease mechanisms (Chang and Grieder 2024) driving discoveries that shape the future of biomedical research.

In this capacity, EMMA plays a vital role in addressing major challenges in biomedical research, such as resource quality, enhancing reproducibility, and promoting ethical animal use. By cryopreserving genetically modified strains, repositories, such as EMMA, reduce the need for continuous live breeding, aligning with the 3Rs principle—Replace, Reduce, Refine—mandated by EU Directive 2010/63/EU (Russell and Burch 1992; Lloyd et al. 2015; Allen et al. 2023) yet not compromising the reproducibility of research

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results. For example, maintaining a single mouse line typically requires around 50 animals annually (Moreno-del Val and Muñoz-Robledano 2019). With approximately 8,900 lines cryopreserved, EMMA helps avoid the breeding of an estimated 445,000 animals each year. Additionally, Moreno-del Val and Muñoz-Robledano (2019) reported that cryopreserving 115 underutilized strains at their institution prevented the production of over 21,000 mice and saved 832,800€, after subtracting the costs for cryopreservation still 382,800€, over five years.

Beyond preservation, EMMA offers not only biological material but also essential metadata, such as genetic background information, to support informed experimental design (Birling et al. 2021). This reference data enables better understanding and comparison of research results, further contributing to high-quality, reproducible, and ethically sound research.

Reproducibility remains a critical issue in science, particularly in preclinical research, where irreproducibility rates range from 51 to 89% (Freedman et al. 2015; Baker 2016). Contributing factors include poor experimental design, genetic drift, and microbiome variability (Justice and Dhillon 2016; Freedman et al. 2017). The financial impact is substantial, with an estimated $28 billion spent annually on irreproducible preclinical research in the U.S. alone (Freedman et al. 2015). This also undermines the translatability of findings to clinical settings (van der Worp et al. 2010).

To address these issues, guidelines such as PREPARE (Smith et al. 2018), ARRIVE ((Kilkenny et al. 2010; Du Percie Sert et al. 2020), and LAG-R (Teboul et al. 2024) have been developed, alongside the FAIR (Findable, Accessible, Interoperable, Reusable) data principles (Wilkinson et al. 2016). EMMA supports these efforts by minimizing genetic drift—a known source of phenotypic variability in genetically altered mice (Justice and Dhillon 2016; Freedman et al. 2017)—through cryopreservation and distribution of rigorously curated, quality-controlled material prepared under standardized protocols.

As Lloyd et al. (2015) aptly stated, “Like money in the bank, repositories keep mouse models safe, secure and available for withdrawal. Just as a bank makes returns on investments, repositories add scientific value and utility to deposited mouse lines: they increase reliability through curation, preservation, genetic quality control, protection from pathogens and more.”

Recognizing the ongoing challenges in biomedical research, INFRAFRONTIER is committed to enhancing the reproducibility and reliability of scientific results in alignment with responsible animal research practices. As part of this commitment, INFRAFRONTIER is implementing internal quality principles across its research areas (Ehlich et al. 2022). They complete existing operational standards with area-specific, fundamental key quality requirements. For EMMA, this includes general aspects such as application of the 3Rs, ensuring staff competence, and continuous improvement aspects but also more topic specific points such as scientific evaluation, data curation, and respecting IP rights, thus guiding the responsible archiving and dissemination of rodent strains through defined protocols and trained personnel.

This article outlines how these quality principles are integrated into EMMA’s workflow, aiming to provide researchers with reliable, ethically sourced models for advancing disease research.

INFRAFRONTIER and EMMA

INFRAFRONTIER (www.infrafrontier.eu) comprises a network of over 20 cutting-edge biomedical research centres across Europe and beyond, offering a range of research services related to disease models to the scientific community, including archiving and distribution of mouse and rat strains through EMMA.

EMMA’s primary objective is to establish and manage a unified repository following highly standardized procedures for maintaining scientifically relevant rodent mutants and making them available to the biomedical research 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 monitoring, extensive curation and dissemination of FAIR, open access genotypic/phenotypic datasets (Ali Khan et al. 2023). Mutant strains are only accepted by EMMA after scientific and technical evaluation, and the level of quality control is always transparently communicated and summarized at www.infrafrontier.eu. The individual archiving and distributing EMMA nodes together with EMMA data curators and external scientific evaluators, work collectively to maintain the quality of the repository. Their efforts are coordinated by the INFRAFRONTIER ERIC (central coordination unit, including Scientific User Support (SUS) and Information Technology (IT) teams).

INFRAFRONTIER Quality Principles in EMMA Archiving and Distribution

To ensure the delivery of high-quality services and their continuous improvement in alignment with the needs and expectations of users and stakeholders, INFRAFRONTIER

employs a structured quality management framework (https://www.infrafrontier.eu/about-us/quality-management/). Within this framework, service specific quality aspects are organized into three complementary tiers: First, detailed, node-specific operational standards; second, common, cross-node operational procedures; and third, the here described overarching quality principles that define general, service-specific key quality requirements.

Following the structure of INFRAFRONTIER's Quality Principles in Systemic Phenotyping (Ehlich et al. 2022), the EMMA Quality Principles (EMMA QPs) were developed collaboratively by the INFRAFRONTIER Quality Management Network Group and representatives from its 11 EMMA nodes. Through this joint effort, 10 core quality aspects were identified as essential to guide EMMA's archiving and distribution activities, and structured into four sections:

- Context—providing background information including specific conditions and circumstances which need to be considered;
- Requirements—specifying mandatory procedures to be implemented at each node;
- Recommendations—offering additional best practices to enhance quality;
- References—listing relevant regulations, publications, and resources for further reading.

Importantly, the EMMA QPs were designed to be adaptable, allowing for flexible implementation across diverse institutional and national contexts while maintaining a consistent quality framework throughout the EMMA network. For example, this adaptability encompasses alignment with national regulatory requirements, accommodation of node-specific procedures, responsiveness to depositor conditions (e.g., delayed data release), the capacity to integrate with external databases, as well as to evolve through iterative improvement cycles tailored to node-specific needs.

While the full-text version of the EMMA Quality Principles is available in the supplemental information (Online Resource 1), the following paragraphs provide a short overview of the principles and highlight selected key elements.

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

All EMMA partners must comply with the Directive 2010/63/EU and its amendments, their national transpositions, and other related regulations. Each EMMA node is primarily subject to the national legislation of its host country and has full flexibility to adapt its modus operandi and operational procedures (see QP 4) accordingly. Compliance includes ethical review procedures, guidance in animal welfare regulations, and adequate training of involved personnel.

QP 2 (3Rs): We promote and apply the ethical and animal welfare principles—3Rs (replacement, reduction, refinement)

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 animals being used for scientific purposes. Duplicated testing is minimized by ensuring visibility and accessibility to strains and associated data. Further internal reduction measures include, but are not limited to, careful management of colony size, the implementation of cryopreservation protocols that minimise the number of animals, and genotyping of blastocysts instead of live mice as a Quality Control (QC) step (Scavizzi et al. 2015). Surgical procedures such as vasectomy and embryo transfer are refined to minimise or alleviate pain, suffering, or distress experienced by the animals. Shipping of frozen samples rather than live animals is promoted to avoid unnecessary stress and anxiety during transport.

QP 3 (GSP): We follow good scientific practices

Measures applied for ensuring data and research integrity, within an EMMA facility and across EMMA nodes, are manifold. These include, inter alia, monitoring of the health status of the mouse and rat strains in line with FELASA recommendations (https://felasa.eu/) (Mähler Convenor et al. 2014), utilisation of validated methods and protocols, recording of data and metadata, recognition of ARRIVE (Kilkenny et al. 2010; Du Percie Sert et al. 2020) and PREPARE (Smith et al. 2018) guidelines, and providing the user with all pertinent information concerning the mouse or rat strains.

QP 4 (SOP): We apply standard operating procedures

Standard Operating Procedures (SOPs) are a key principle to ensure transparency and consistent quality for reproducible research results. All nodes are advised to implement and maintain node-specific SOPs for EMMA procedures (archiving, quality control, distribution), thereby allowing flexibility to implement methods that align with local circumstances while ensuring optimal outcomes.

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

Each EMMA node activity requires adequately qualified and trained personnel in order to ensure that procedures are performed in a reproducible manner and generate consistent high-quality results. It is imperative to ensure that job requirements and responsibilities are clearly defined and that all employees acquire and maintain the competence and skill level to perform techniques to a satisfactory standard.

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

Users of EMMA archiving and distribution services are scientists who either wish to deposit or obtain mutant rodent strains. Our communication policy aims at transparency which includes clearly stating what the user can expect from the requested EMMA service, in particular with regard to any limitations, and informing the user as soon as possible in case of unexpected delays or issues. We aim to respond to all types of requests, including complaints, in a timely manner.

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

EMMA's ambition is to provide access to valuable rodent mutant strains with significance for current and future biomedical research. To ensure this, strains submitted to EMMA undergo an evaluation process which includes an external scientific assessment based on the provided information. The main evaluation criteria are: sound scientific methods, evidence of heritability, identifiable genotype, and stabilised phenotype. Transparency of the evaluation results is ensured through the completion of an evaluation form by the external evaluators, and the evaluation criteria are made available to users via the INFRAFRONTIER website.

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

EMMA services are generally available to all scientists working in academic research; access for industry is possible if strain owner and requester agree on individual terms of transfer. When a strain is deposited at EMMA, the intellectual property (IP) and the ownership of the material remain with the depositor. INFRAFRONTIER/EMMA only acts as a coordinator and broker. Any existing Material Transfer Agreement (MTA) shall remain in full force. EMMA legally binding general conditions must be accepted in order to receive the requested service. Depositors are required to either be the sole owner of the allele/strain or have permission from all owners. A grace period may be granted, if necessary. This provides the depositors with the flexibility to publish a newly created strain before it is available on the INFRAFRONTIER website.

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

INFRAFRONTIER-EMMA has been reviewed, selected, and listed as a FAIR-compliant resource by the reference FAIRsharing International Consortium (https://fairsharing.org/). As a means of ensuring that EMMA data are FAIR-fied, each strain submitted to EMMA undergoes standardised data curation procedures which include strain nomenclature and assignment of background(s)/gene(s)/mutation type(s)/allele(s)/transgene(s) attributes according to the rules and guidelines of the International Committee on Standardized Genetic Nomenclature for Mice (https://www.informatics.jax.org/mgihome/nomen/index.shtml). The curated records are associated with unique, persistent numeric identifiers as defined by respective reference resources (e.g., Mouse Genome Informatics (MGI), International Mouse Strain Resource (IMSR), ORPHANET, Disease Ontology). This enables flexible integration and streamlined cross-referencing of INFRAFRONTIER-EMMA datasets, enhancing their findability, accessibility, and international dissemination.

To comply with data protection requirements all users of the EMMA repository service must agree to the EMMA data privacy policy.

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

Improvement is a fundamental concept embedded in established quality management standards such as ISO 9001, AAALAC, and Good Laboratory Practice (GLP). In order to continuously improve the processes at INFRAFRONTIER / EMMA, we conduct cross-centre exchange of experience through dedicated working groups. Customer feedback is regularly solicited through common EMMA feedback forms and recorded centrally along with other service performance indicators such as number of strains archived/shipped. Procedures should be implemented to monitor local processes against the INFRAFRONTIER quality principles and the quality objectives set by the EMMA node. As an

outcome, action plans will be defined to support continuous improvement.

EMMA Workflow

The EMMA workflow encompasses standardized procedures for the cryo-archiving and worldwide distribution of mutant mouse and rat strains, which are submitted and requested by scientists globally (Fig. 1). Activities are carried out by well-trained staff at EMMA nodes, with centralized support from the INFRAFRONTIER ERIC.

Strain deposition and archiving

Scientists who own, or have permission from all owners of a mutant strain can submit it to EMMA through the EMMA online submission form (https://services.infrafrontier.eu/submissionForm/#!submissionTermsView). Before starting the submission, submitters need to agree to the EMMA repository conditions and the data privacy statement. Following they are required to provide comprehensive strain information with a complete description of the strain's genetic and phenotypic characteristics, including genetic background, specific applications in disease modelling, and relevant scientific publications describing the generation or use of the strain. Once the online form is completed and submitted, an automated confirmation is sent to the contacts provided in the form.

The SUS team reviews each submission for completeness and may contact the submitter if clarifications or additional information are needed. This may relate to details such as the genotyping protocol, IP right restrictions, MTAs, animal health reports, or similar documentation. The SUS team then initiates the evaluation by at least one member of the INFRAFRONTIER External Scientific Evaluation Committee who assesses the scientific relevance and quality of the strain. The process is guided by the Quality Principles QP 4 (SOP), QP 5 (Staff), QP 6 (Interaction), QP 7 (Evaluation) and QP 8 (IP Rights).

Database curators and the IT team ensure that all relevant data/metadata of the strain are captured in the INFRAFRONTIER database in compliance with FAIR data principles, including correct assignment of a unique EMMA ID and a Research Resource Identification ID (RRID), standard nomenclature, and integration with external resources (MGI-IMSR, International Mouse Phenotyping Consortium (IMPC), ORPHANET, Disease Ontology, etc.), following QP 4 (SOP), QP 5 (Staff) and QP 9 (FAIR Data).

Upon acceptance, the depositor, directed by EMMA's SUS team, usually sends live animals to the national or geographically nearest EMMA node. If plausible, refrigerated or frozen germplasm materials can also be used for this shipment (QP 1 (Legislation), QP 2 (3Rs), QP 6 (Interaction)).

At the EMMA node, the strain is cryopreserved using the EMMA-validated, most advanced methods and protocols, and the genotype and cryobiological quality of the frozen material is checked (QP 3 (GSP), QP 4 (SOP), QP 5 (Staff)). Careful quality control measures, such as blastocyst genotyping for allele verification and continuous hygiene monitoring of all animal facilities, ensure the integrity and reliability of the cryopreserved material (QP1 (legislation), QP3 (GSP)).

The strain is then searchable via the public INFRAFRONTIER/EMMA website (https://www.infrafrontier.eu), with its associated data/metadata, as well as material transfer agreement (MTA) documentation, if required by the strain owner (QP 8 (IP Rights), QP 9 (FAIR Data)).

Strain distribution

Researchers can browse and order EMMA strains directly via the INFRAFRONTIER website (https://www.infrafrontier.eu) or via other public portals, e.g. IMSR (https://www.findmice.org/) and RRID (https://rrid.site/) sites (QP 9 (FAIR Data)). As needed, the SUS team provides support (QP 6 (Interaction)), for example in response to questions regarding cost estimation and service timeframes, genetic background of archived strains, type and quantity of cryopreserved materials, access conditions for industry users, or availability of specific strains for particular mutations or disease models.

Incoming strain orders are routed directly to the EMMA node that holds the respective strain, as well as to the SUS team. As needed, the SUS team may contact the requester to clarify open questions or assist with specific requirements, e.g. breeding of requested strains, allele conversion of IMPC strains, rederivation of live animals by 3rd party service provider, or licensing agreement for industry. The provision of necessary documents and information is coordinated in direct exchange with the requester by the responsible Archive Manager at the selected EMMA node (QP 1 (Legislation), QP 6 (Interaction), QP 8 (IP Rights)).

EMMA strongly encourages the shipment of frozen material. If the receiving scientist orders rederived live animals, the EMMA node points out the advantages of sending frozen samples over live animals. Using frozen material avoids the stress, health risks, and potential mortality associated with transporting live animals (QP 2 (3Rs)). If receiving frozen material is not an option, live animals are rederived using the EMMA-validated protocols and are shipped following required genetic and hygiene checks (QP 1 (Legislation), QP 3 (GSP), QP 4 (SOP), QP 5 (Staff)).

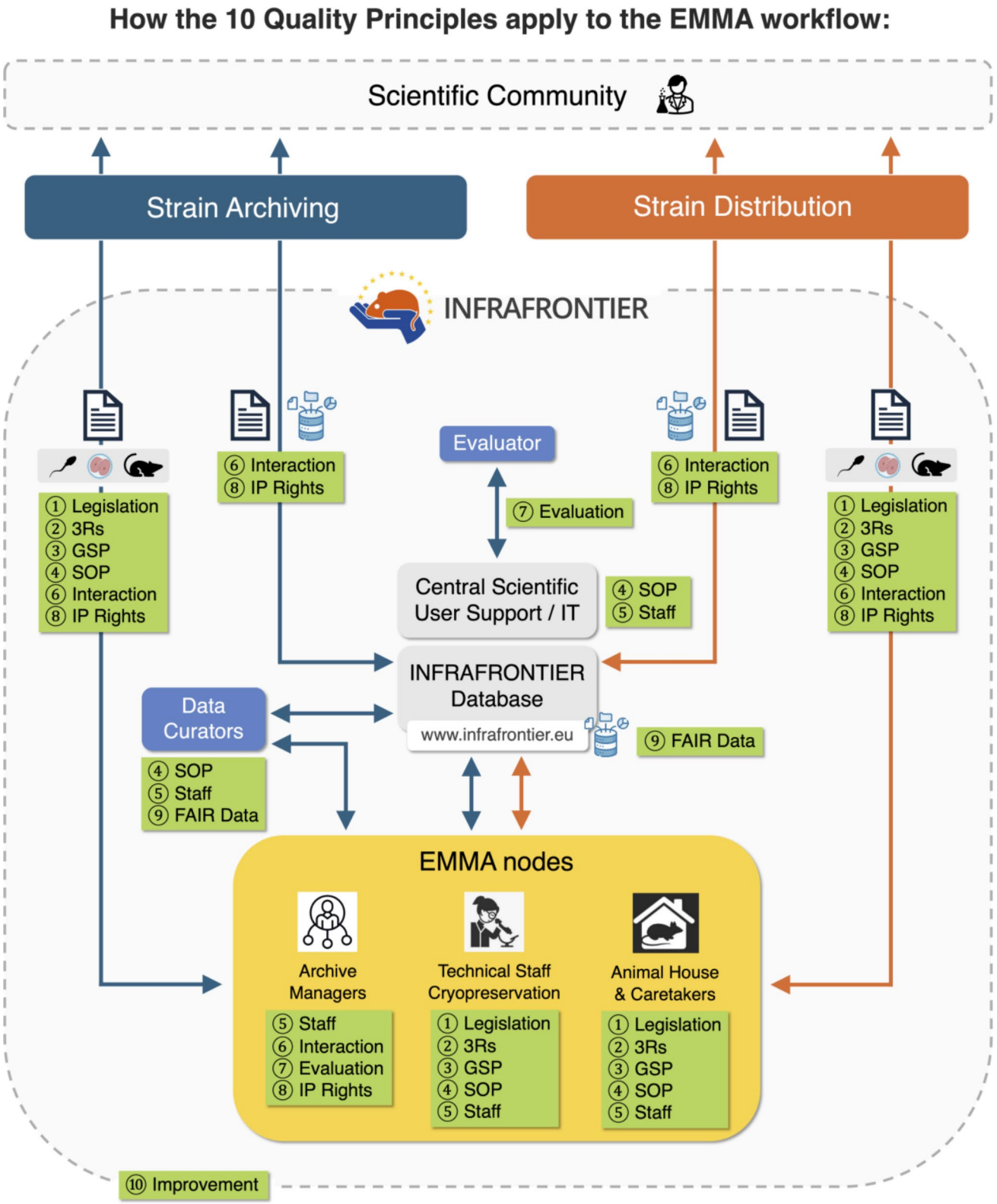

Fig. 1 Schematic representation of the EMMA workflow, illustrating the application of the 10 EMMA Quality Principles in the procedures for archiving and distribution of mutant rodent strains. As detailed in the text, these principles guide both the deposition of mutant strains and the global distribution to the scientific community. Applicable QPs are displayed as green boxes with QP number and keyword

Shipping is coordinated with care by individual EMMA nodes together with the user's selected courier service provider and the receiving institution. This is done to minimize stress and risk during transport, ensuring compliance with ethical and legal requirements while maintaining efficiency (QP 1 (Legislation), QP 2 (3Rs), QP 6 (Interaction)).

Cross-cutting aspects

After deposition or distribution, both donating and receiving scientists are invited to provide feedback through an online form to share their experiences with the EMMA procedures. This feedback supports ongoing improvements in INFRAFRONTIER's operations and quality management (QP 10 (Improvement)).

Cross-node operational standards are defined in the EMMA Operational Handbook, which serves as an internal reference document. Staff from all EMMA nodes, including data curators, SUS, and IT teams, participate in EMMA and related projects meetings to ensure consistent application of operational standards. These meetings support knowledge sharing, user feedback evaluation, and the development or updating of procedures as needed, contributing to continuous quality improvement (QP 10).

EMMA Archive Managers and the SUS team coordinate interactions with external users and between EMMA nodes, and handle IP right matters related to strain deposition or export (QP 6 (Interaction), QP 8 (IP Rights)). Staff members involved in EMMA procedures such as cryopreservation, revitalization, and animal care, follow EMMA protocols and applicable SOPs (QP 4 (SOP)) in line with European/national legislation on animal protection (QP 1 (Legislation)), 3Rs ethical principles (QP 2 (3Rs), and good scientific practices (QP 3 (GSP)). They maintain high professional competence through regular training, compliant with European/national legislations (QP 5 (Staff)).

The INFRAFRONTIER QPs for EMMA Archiving and Distribution are integrated into all aspects of the EMMA workflow, ensuring the establishment and maintenance of appropriate operational standards. These standards are essential for delivering high quality services and materials, thereby supporting the global scientific community.

Conclusion

The Quality Principles in EMMA Archiving and Distribution outlined in this paper constitute a foundational element in advancing EMMA's overarching mission: to provide the scientific community with access to reliable, scientifically validated mutant rodent strains. They not only support the reproducibility and robustness of biomedical research but also contribute significantly to the ethical imperative of the 3R principle, by promoting animal welfare, minimizing unnecessary duplication and ensuring the integrity of archived resources.

By articulating clear and actionable quality criteria, these principles provide an effective framework that enables quality-oriented guidance of workflows within centrally coordinated yet decentralized cryo-archives such as EMMA. The structured approach fosters a culture of quality assurance and continuous improvement, ensuring that operational practices remain aligned with evolving scientific standards and community expectations.

The principles are also designed with flexibility in mind, allowing for adaptation to diverse national and institutional regulatory environments. This adaptability ensures broad applicability across different jurisdictions while maintaining a consistent baseline of quality.

Looking ahead, these Quality Principles may lay the groundwork for future harmonization efforts across different biobanking infrastructures. Their implementation could pave the way for increased interoperability and data sharing, ultimately amplifying the impact of biobanked resources on scientific discovery and innovation.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

References

Ali Khan A, Valera Vazquez G, Gustems M, Matteoni R, Song F, Gormanns P, Fessele S, Raess M, Hrabě de Angelis M (2023) INFRAFRONTIER: mouse model resources for modelling human diseases. Mamm Genome 34:408–417. https://doi.org/10.1007/s00335-023-10010-7

Allen S, Summerfield R, Fray M (2023) Why use a biobank? Sharing mutations, gene editing and navigating the COVID-19 pandemic. MRAJ. https://doi.org/10.18103/mra.v11i6.3871

Baker M (2016) 1,500 scientists lift the lid on reproducibility. Nature 533:452–454. https://doi.org/10.1038/533452a

Birling M-C, Fray MD, Kasparek P, Kopkanova J, Massimi M, Matteoni R, Montoliu L, Nutter LMJ, Raspa M, Rozman J, Ryder EJ, Scavizzi F, Voikar V, Wells S, Pavlovic G, Teboul L (2021) Importing genetically altered animals: ensuring quality. Mamm Genome 33:100–107. https://doi.org/10.1007/s00335-021-09908-x

Chang MCJ, Grieder FB (2024) The continued importance of animals in biomedical research. Lab Anim (NY) 53:295–297. https://doi.org/10.1038/s41684-024-01458-4

Du Percie Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, Browne WJ, Clark A, Cuthill IC, Dirnagl U, Emerson M, Garner P, Holgate ST, Howells DW, Karp NA, Lazic SE, Lidster K, MacCallum CJ, Macleod M, Pearl EJ, Petersen OH, Rawle F, Reynolds P, Rooney K, Sena ES, Silberberg SD, Steckler T, Würbel H (2020) The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. PLoS Biol 18:e3000410. https://doi.org/10.1371/journal.pbio.3000410

Ehlich H, Cater HL, Flenniken AM, Da Goncalves Cruz I, Mura A-M, Ntafis V, Raess M, Selloum M, Stoeger C, Suchanova S, Vuolteenaho R, Brown SDM, Hérault Y, Hinttala R, de Hrabě Angelis M, Kollias G, Kontoyiannis DL, Malissen B, McKerlie C, Sedláček R, Wells SE, Zarubica A, Rozman J, Sorg T (2022) INFRAFRONTIER quality principles in systemic phenotyping. Mamm Genome 33:120–122. https://doi.org/10.1007/s00335-021-09892-2

Freedman LP, Cockburn IM, Simcoe TS (2015) The economics of reproducibility in preclinical research. PLoS Biol 13:e1002165. https://doi.org/10.1371/journal.pbio.1002165

Freedman LP, Venugopalan G, Wisman R (2017) Reproducibility2020: progress and priorities. F1000Res 6:604. https://doi.org/10.12688/f1000research.11334.1

INFRAFRONTIER Consortium (2015) INFRAFRONTIER--providing mutant mouse resources as research tools for the international scientific community. Nucleic Acids Res 43:D1171–D1175. https://doi.org/10.1093/nar/gku1193

Justice MJ, Dhillon P (2016) Using the mouse to model human disease: increasing validity and reproducibility. Dis Model Mech 9:101–103. https://doi.org/10.1242/dmm.024547

Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG (2010) Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research. PLoS Biol 8:e1000412. https://doi.org/10.1371/journal.pbio.1000412

Lloyd K, Franklin C, Lutz C, Magnuson T (2015) Reproducibility: use mouse biobanks or lose them. Nature 522:151–153. https://doi.org/10.1038/522151a

Mähler Convenor M, Berard M, Feinstein R, Gallagher A, Illgen-Wilcke B, Pritchett-Corning K, Raspa M (2014) FELASA recommendations for the health monitoring of mouse, rat, hamster, guinea pig and rabbit colonies in breeding and experimental units. Lab Anim 48:178–192. https://doi.org/10.1177/0023677213516312

Moreno-del Val G, Muñoz-Robledano P (2019) Cryopreservation of genetically modified mouse strains: preserving valuable material, saving resources and reducing animal usage. Scand J Lab Animal Sci. https://doi.org/10.23675/sjlas.v45i0.607

Raess M, Castro AAde, Gailus-Durner V, Fessele S, de Hrabě Angelis M (2016) INFRAFRONTIER: a European resource for studying the functional basis of human disease. Mamm Genome 27:445–450. https://doi.org/10.1007/s00335-016-9642-y

Russell WMS, Burch RL (1992) The principles of humane experimental technique, 1959th edn. Universities Federation for Animal Welfare, Potters Bar, Herts

Scavizzi F, Ryder E, Newman S, Raspa M, Gleeson D, Wardle-Jones H, Montoliu L, Fernandez A, Dessain M-L, Larrigaldie V, Khorshidi Z, Vuolteenaho R, Soininen R, André P, Jacquot S, Hong Y, Angelis MHde, Ramirez-Solis R, Doe B (2015) Blastocyst genotyping for quality control of mouse mutant archives: an ethical and economical approach. Transgenic Res 24(5):921–927. https://doi.org/10.1007/s11248-015-9897-1

Smith AJ, Clutton RE, Lilley E, Hansen KEA, Brattelid T (2018) Prepare: guidelines for planning animal research and testing. Lab Anim 52:135–141. https://doi.org/10.1177/0023677217724823

Teboul L, Amos-Landgraf J, Benavides FJ, Birling M-C, Brown SDM, Bryda E, Bunton-Stasyshyn R, Chin H-J, Crispo M, Delerue F, Dobbie M, Franklin CL, Fuchtbauer E-M, Gao X, Golzio C,

Haffner R, Hérault Y, de Hrabe Angelis M, Lloyd KCK, Magnuson TR, Montoliu L, Murray SA, Nam K-H, Nutter LMJ, Pailhoux E, de Pardo Manuel Villena F, Peterson K, Reinholdt L, Sedlacek R, Seong JK, Shiroishi T, Smith C, Takeo T, Tinsley L, Vilotte J-L, Warming S, Wells S, Whitelaw CB, Yoshiki A, Pavlovic G (2024) Improving laboratory animal genetic reporting: LAG-R guidelines. Nat Commun 15(1):5574. https://doi.org/10.1038/s41467-024-49439-y

van der Worp HB, Howells DW, Sena ES, Porritt MJ, Rewell S, O'Collins V, Macleod MR (2010) Can animal models of disease reliably inform human studies? PLoS Med 7(3):e1000245. https://doi.org/10.1371/journal.pmed.1000245

Wilkinson P, Sengerova J, Matteoni R, Chen C-K, Soulat G, Ureta-Vidal A, Fessele S, Hagn M, Massimi M, Pickford K, Butler RH, Marschall S, Mallon A-M, Pickard A, Raspa M, Scavizzi F, Fray M, Larrigaldie V, Leyritz J, Birney E, Tocchini-Valentini GP, Brown S, Herault Y, Montoliu L, Angelis MHde, Smedley D (2010) EMMA--mouse mutant resources for the international scientific community. Nucleic Acids Res 38:D570–D576. https://doi.org/10.1093/nar/gkp799

Wilkinson MD, Dumontier M, Aalbersberg IJJ, Appleton G, Axton M, Baak A, Blomberg N, Boiten J-W, Da Silva Santos LB, Bourne PE, Bouwman J, Brookes AJ, Clark T, Crosas M, Dillo I, Dumon O, Edmunds S, Evelo CT, Finkers R, Gonzalez-Beltran A, Gray AJG, Groth P, Goble C, Grethe JS, Heringa J, Hoen PAC't, Hooft R, Kuhn T, Kok R, Kok J, Lusher SJ, Martone ME, Mons A, Packer AL, Persson B, Rocca-Serra P, Roos M, van Schaik R, Sansone S-A, Schultes E, Sengstag T, Slater T, Strawn G, Swertz MA, Thompson M, van der Lei J, van Mulligen E, Velterop J, Waagmeester A, Wittenburg P, Wolstencroft K, Zhao J, Mons B (2016) The FAIR guiding principles for scientific data management and stewardship. Sci Data 3:160018. https://doi.org/10.1038/sdata.2016.18

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