A framework for quality management in the biomedical research infrastructures (BMS RIs)

BMS RIs put quality at the heart of biomedical research

It has been widely recognized that the proper use of verified reference materials, standard operation protocols, study designs and data analysis and data storage is crucial to increase the **quality of biomedical research** and reduce the **waste of resources that comes with irreproducible results**[1].

The **continuous development of community standards and references** in the area of biomaterial and reagents, technology platforms, operations procedures, data collection and data processing is a **core activity of the biomedical research infrastructures (BMS RIs)** that are recognized as ESFRI Projects or ESFRI Landmarks[2] (see also '*Who are the BMS RIs?'* further below).

In order to ensure that these standards are widely and consistently applied**, the BMS RIs all endorse the methodologies and underlying mind set of quality management**. They apply quality management systems that ensure that the resources and services that they offer to the European biomedical research community are of highest quality, produce reliable, traceable and reproducible outputs that are consistent across centers and are compliant with the regulatory environment. Since **BMS RIs are distributed with partners in several European countries**, quality management systems are applied or in the case of being defined at both

[1] e.g. Freedman et al. 2015. The Economics of Reproducibility in Preclinical Research. PLoS Biology, 13(6), e1002165.

[2] http://www.esfri.eu

the central coordination hubs and at the sites that provide the infrastructure resources and services.

This creates a win-win situation for all the actors and stakeholders in the biomedical research field: **public funders** profit from the BMS RI contribution to increased reproducibility and decrease wasting of public resources, **publishers and peer-reviewed journals** and **users from academia and industry** can rely on the high-quality of outputs based on BMS RI resources and services. Ultimately this will contribute to a more efficient delivery of drugs and treatments to **address the societal health challenges**.

Common BMS RI principles for quality management

The BMS RIs offer a **wide portfolio of resources and services**, ranging from access to biomaterials, technological platforms, databases, data analysis, expertise and consulting. Therefore, there is **no one-size-fits-all solution** for quality assurance and control that is applied by all BMS RIs. However, they all **share a core set of principles**:

1. The BMS RIs recognize that **standardisation** is the basis for reproducible and traceable results in science. They therefore acknowledge and actively pursue their important role in cataloguing, developing, improving and widely disseminating community standards.
2. The BMS RIs strive to **apply quality management methodology** to all of their core activities, thus ensuring highest-quality services and data to enable highest-quality science.
3. The BMS RIs acknowledge that **open access to research data** is an important quality measure.
4. The BMS RIs acknowledge that an independent assessment by a competent authority is the gold standard for quality assurance.
5. The BMS RIs strive to **use internationally recognised standards** (e.g. ISO, CEN) and best practices (e.g. OECD Best Practice Guidelines for Biological Resource Centres) where applicable. They are also committed to actively engage in the development of internationally recognised standards where appropriate.
6. The BMS RIs represent a wide area of expertise in the biomedical sciences. They recognize that **pooling all their best-practice examples and guidelines in a shared resource** provides great value for further improving the quality management in each individual BMS RI.
7. The BMS RIs acknowledge the **importance of training of quality management methodology** for research infrastructures and their users. They therefore include the topic of quality assurance and quality control into their training activities wherever appropriate.
8. The BMS RIs recognize the importance of actively engaging with all other stakeholders (e.g. public funders, journals or users) to **create awareness and appraisal for quality management** as a central tenet in biomedical research. This is best done by clearly communicating how the application of quality measures by the BMS RIs contributes to improving the biomedical research outputs.

Who are the BMS RIs?

Thirteen biomedical research infrastructures on the ESFRI roadmap develop this common *framework for quality control and quality assurance* in the context of the CORBEL project (www.corbel-project.eu). CORBEL aims to create a platform for harmonised user access to biological and medical technologies, biological samples and data services required by cutting-edge biomedical research.

BBMRI-ERIC - Biobanking and BioMolecular Resources Research Infrastructure – European Research Infrastructure Consortium

www.bbmri-eric.eu

BBMRI-ERIC aims to improve the accessibility and interoperability of the existing comprehensive collections, either population-based or clinical-oriented, of biological samples from different (sub-) populations of Europe or rare diseases. These collections include the attached data on factors such as health status, nutrition, lifestyle, and environmental exposure of the study subjects.

The key benefits for users of BBMRI-ERIC are fair access to quality-controlled samples and/or data from population-based, disease-oriented or rare disease biobanks including expertise in handling these biological resources for scientific purposes (ethical, legal and societal issues as well as quality handling). BBMRI-ERIC connects a distributed research infrastructure of biobanks and biomolecular resources for the benefit of the users of such resources.

EATRIS - European Infrastructure for Translational Medicine

www.eatris.eu

EATRIS is the European infrastructure for translational medicine, providing high quality services in early development of novel therapeutics and diagnostics. Translational research is defined as research that develops promising biomedical innovations 'from bench to bedside,' and conversely brings clinical insights from bedside back to bench.

The wide-ranging services portfolio focuses on supporting early decision-making and de-risking of projects. Examples include validation and development of in vitro and in vivo biomarkers for patient stratification, molecular imaging tracers for drug development programmes, GMP manufacturing of cellular therapy products[3], patient-derived xenograft models, and many more highly specialised capabilities.

[3] EudraLex - Volume 4 - Good Manufacturing Practice (GMP) guideline
http://ec.europa.eu/health/documents/eudralex/vol-4_en

EATRIS is an open access, non-profit European Research Infrastructure Consortium (ERIC). Member institutions are selected on the basis of their track record in public-private collaboration in translational development and their multidisciplinary teams of leading academic experts, high-end research facilities, production laboratories and licenses.

ECRIN - European Clinical Research Infrastructure Network

www.ecrin.org

ECRIN focuses on multinational clinical research initiated by academic sponsors as well as biotech and medical device small and medium enterprises (SMEs). Multi-country trials means greater access to patients, resources, and expertise, and, in turn, faster and potentially more robust results.

ECRIN provides support for the preparation of multinational clinical trials (e.g., trial logistics, funding applications), the assessment and validation of study methodology and protocols (scientific and logistical review), and trial management (coordination and support for submissions to competent authorities and ethics committees, monitoring, adverse event reporting, data management). In addition, ECRIN develops and maintains freely accessible tools such as databases on regulatory and ethical requirements, outcome measures, and risk-based monitoring. ECRIN currently provides consultancy and management services to more than 40 trials, with an average of seven countries per trial.

ECRIN applies high level quality standards for its organisation, provides quality as a service to ECRIN external stakeholders (data centres certification) and shares cross-functional quality expertise to enhance biomedical research structuring and robustness.

ELIXIR

www.elixir-europe.org

ELIXIR is a European research infrastructure to coordinate the collection and stewardship of the increasing volume of data generated by life science experiments.

ELIXIR unites Europe's leading life science organisations and enables researchers in academia and industry to access vital data, tools, standards, compute and training services for their research. As a distributed infrastructure with 21 ELIXIR Nodes across Europe (20 national Nodes and EMBL-EBI); ELIXIR offers hundreds of bioinformatics services supporting every aspect of 'big data' biology.

The application areas supported by ELIXIR are broad and cover disciplines including marine metagenomics, plant sciences, human data, rare diseases, systems biology, cheminformatics and others.

EMBRC - European Marine Biological Resource Centre

www.embrc.eu

The EMBRC-ERIC is a pan-European distributed research infrastructure that aims to provide a strategic delivery mechanism for excellent and large-scale marine biological and ecological research in Europe. With its services, EMBRC will support both fundamental and applied research based on marine bioresources and ecosystems. In particular, EMBRC aims to drive forward the development of blue biotechnologies.

Catering for users from academia, industry, policy and the technology sectors, EMBRC provides a unique entry point to access an integrated portfolio of services, bio-technology research platforms and marine organisms, as well as analytical and historical environmental data, to investigate the potential of the marine bioresources to deliver for societally relevant research domains.

EMPHASIS - European Infrastructure for Multi-Scale Plant Phenotyping And Simulation for Food Security in a Changing Climate

https://emphasis.plant-phenotyping.eu/

EMPHASIS is a pan-European, ESFRI listed plant phenotyping infrastructure project. The project has started the preparatory phase that will provide the basis for the establishment the legal framework, the business plan and preparation of an information system for a sustainable and innovative pan-European infrastructure for plant phenotyping.

EMPHASIS will focus on developing and enabling access to plant phenotyping infrastructure and provision of services essential for the analysis of crop performance with respect to structure, function, quality and interaction with the environment, which is essential for the exploitation of crop genetic diversity required for the enhancement of plant productivity and progress in plant breeding.

ERINHA – European Research Infrastructure on Highly Pathogenic Agents

http://www.erinha.eu/

ERINHA is dedicated to the study of highly infectious emerging and re-emerging diseases classified as Risk Group 4 (RG4).

The infrastructure provides the expertise, capacities and functions required to lead or support research studies into human diseases caused by the most highly pathogenic agents, as well as applied research to develop new countermeasures and other interventions against these diseases. The RI provides access to cutting edge research facilities including BSL-4 in vitro capacities and in-vivo unique capacities to perform animal experimentations (from mice to NHP) thus allowing excellent science to be performed.

A pool of trained specialists to perform research as well as renowned senior scientists is part of ERINHA. The infrastructure will contribute to the enhancement of the European and global capacity, capability and emergency preparedness in the response to global outbreaks and thus will constitute a key European contribution to the global health research and innovation.

ERINHA-AISBL moves towards implementation from July 2017. Its Central Coordinating Unit which ensures access to the RI is hosted in Paris, France.

EU-OPENSCREEN - European Infrastructure of Open Screening Platforms for Chemical Biology

www.eu-openscreen.eu

EU-OPENSCREEN integrates high-capacity screening platforms throughout Europe, which jointly use a rationally selected compound collection, comprising up to 140.000 commercial and proprietary compounds collected from European chemists.

The use of shared EU-OPENSCREEN resources will enable the development of novel molecular tool compounds in collaboration with external researchers from various disciplines of the life sciences. All generated tool compounds and data will be made available in an open access database.

EU-OPENSCREEN supports all stages of a tool development project, including assay adaptation, high-throughput screening, and chemical optimisation of the ‘hit’ compounds and targets researchers from academic institutions, SMEs and industrial organisations. Chemists are encouraged to include their compounds into the EU-OPENSCREEN compound collection which is screened against a wide range of biological assays, thereby delivering extensive information about the biological activities of their compounds. Scientists or consortia applying for grants and aiming to screen for chemical tools are invited to contact EU-OPENSCREEN for support.

Euro-BioImaging

www.eurobioimaging.eu

Euro-BioImaging (EuBI) is the pan-European Research Infrastructure project on the ESFRI roadmap which will provide access to state-of-the-art imaging technologies for life scientists. Innovative imaging technologies are revolutionizing biology and medicine by allowing researchers to visualize, characterize and measure molecular and cellular function with a precision never reached before.

Through EuBI, researchers can have access to imaging instruments and expertise that they do not find at their home institutions or among their collaboration partners. In addition, EuBI users will receive expert technical assistance and support both with project planning and during project execution. EuBI will offer image data support and training for infrastructure users and providers, as well as continuously evaluating and acquiring new imaging technologies to ensure the sustained delivery of cutting-edge services.

INFRAFRONTIER - the European research infrastructure for the development, phenotyping, archiving and distribution of mammalian models

www.infrafrontier.eu

INFRAFRONTIER advances the understanding of human health and disease by providing access to centralised high-quality resources and data for the development, phenotyping, archiving and distribution of mammalian models. Access is provided for individual researchers and for national, European and international research programmes. INFRAFRONTIER serves a global user community.

INFRAFRONTIER's comprehensive first-line systemic phenotypic analysis covers the entire organism, ranging from cardiovascular, neurology, behaviour and metabolism screens to detailed pathology assessments. The European Mouse Mutant Archive (EMMA) is a non-profit repository for maintaining medically relevant mouse mutants and making them available to the scientific community. EMMA is the largest mouse repository in Europe and the third-largest non-profit mouse archive worldwide, it provides access to over 6000 mutant mouse lines. INFRAFRONTIER sets and applies common standard operation procedures, quality measures and data standards. Best practices are shared by making all related information available through the INFRAFRONTIER web portal and in regular training courses.

Instruct – Integrating Structural Biology

www.structuralbiology.eu

Structural biology is one of the key frameworks on which we interpret molecular and cellular functions. The main experimental technologies are complementary, and increasingly link detailed atomic structure with cellular context. Structural biology is currently in the middle of a revolution enabled by significant advances in the tools (direct electron detectors in EM, advances in synchrotron sources and detectors, XFEL, ultra-high field NMR, super-resolution cryo-light microscopy). Instruct, now adopted as a European Research Infrastructure Consortium (ERIC), is the major European research infrastructure in structural biology with special focus on making high-end technologies and methods available to academic and commercial users.

Instruct offers a coordinated route to access each of the Instruct technologies appropriate for the best scientific outcome: this takes the form of peer-reviewed, free-at-the-point-of-use, open access with expert support and supervision with advice on other methods, technologies or approaches that might be useful to achieve a good scientific outcome.

ISBE - Infrastructure for Systems Biology Europe

http://project.isbe.eu

ISBE is a knowledge-based research infrastructure that will empower European researchers across academia, clinics and industry to implement systems biology approaches addressing how the dynamic interactions between biological components (molecules, cells, tissues, organs) leads to the functioning of living organisms.

ISBE will actively support scientists in facilitating model-compliant data generation, accessing resources for storing and sharing research assets, making their research assets FAIR compliant (that is findable, accessible, interoperable, and reusable) and creating predictive computational multi-scale models of biological systems based on integration of highly diverse data sets. In addition, ISBE will provide training for infrastructure users and providers to offer efficient services.

MIRRI - Microbial Resource Research Infrastructure

www.mirri.org

MIRRI integrates the main microbial domain Biological Resource Centres (mBRCs) and their supporting services and data into a novel pan-European coordinated research infrastructure.

MIRRI partners, currently 12 mBRCs from 11 countries, provide to users from academia, health and agriculture authorities and the bio-industry a broad range of microorganisms (about 450,000 resources):. bacteria (including cyanobacteria), archaea, fungi, yeasts, plant viruses, bacteriophages and their isolated DNA as well as human, animal and plant cell cultures.

In addition to their collection activity, mBRCs offer their unrivalled expertise in the analysis of complex microbial interactions, ranging from isolation of a specimen from the environment to description of novel species, deciphering the genomic information and its path from genes to expressed phenotypes. Targeted identification of genes of interest for biotechnological exploitation as well as analysis of ‘microbiomes’ make MIRRI mBRCs interesting partners not only for academic researchers but also for industry and ‘personalized medicine’.