ADOPT BBMRI-ERIC
gateway for health

ADOPT BBMRI-ERIC
GRANT AGREEMENT NO. 676550

DELIVERABLE REPORT

Deliverable no	D7.3
Deliverable Title	Harmonised Quality Standards
Contractual delivery month	M24 (September 2017)
Responsible Partner	BBMRI-ERIC
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HARMONISED QUALITY STANDARDS

Executive Summary

Part of the WP7 work on Rare Diseases (RD) is to define specific quality standards for samples and data in the context of RD. These quality standards are to match with requirements of BBMRI-ERIC while being compliant with the criteria and procedures of existing RD biobanks.

Based on the discussions of RD Working Group of BBMRI-ERIC, the quality standards recommended by quality groups such as BBMRI-ERIC as well as those Standard Operating Procedures of EuroBioBank should be followed in regards of sample quality. The new developments are done by BBMRI-ERIC operating as an observer liaison with the ISO/TC 276 and ISO/TC 212, which enables BBMRI-ERIC to follow and contribute to the development of ISO standard for biobanks. BBMRI-ERIC is also a partner of the SPIDIA4P project by which new CEN/TC are being developed for personalized medicine. Hence, BBMRI-ERIC is taking its key role in facilitating pan-European supply of good sample quality by operating as the information hub for the latest developments in the sample quality standards and supporting the implementation of the new quality standards within the biobanks in Europe.

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1. Background

BBMRI-ERIC Quality Service encourages the biobanks to comply with the highest quality requirements available to serve the best interests of users. Quality System (QS) within a biobank should cover the whole operational management, including the quality assessment/quality control of samples and data. BBMRI-ERIC recommends the QS for sample management to follow best practice guidelines such as those of the OECD, BBMRI Quality Policy and applicable European standards for pre-analytical treatment of biological samples. Quality standards is the key to reducing the number of samples based diagnostic mistakes, reducing the number of non-reproducible pre-clinical and clinical studies, and enabling the improvement and speeding of discoveries e.g. in the biomarker field.

The best approach for the RD field in regards of quality is to apply and benefit of the quality criteria and standards that are developed or being developed for the biobanks in general. However, for certain rare diseases, European Reference Networks can play a crucial role in the future for providing the expertise needed for small patient populations scattered across the Europe.

This report compiles the recommendations of BBMRI-ERIC in regards of quality that may be of relevance to the RD community.

2. Recommendations for quality

The use of best practices and quality standards in RD field is, similar to any other biobanking area, dependent of the sample type in question, data linked to it and the intended research use. Considering the preciousness due to their scarcity, it is if anything even more important to adhere to widely accepted quality standards to advance data reusability. A rapidly expanding set of quality assessment and management guidelines is currently being developed internationally, most of which will apply to common and rare disease samples and data alike:

2.1 Quality Standards (QS) – Recommendations from BBMRI-ERIC[1]

Applicable Quality Management Systems (QMS) for biobanks

BBMRI-ERIC Quality Policy

- OECD best practice guidelines for Biological Resource Centres
- WHO/IARC guidelines for biological resource centres for cancer research

BBMRI-ERIC recommended International Standards

- ISO 9001:2008 Quality management systems – Requirements
- ISO 15189:2012 Medical laboratories – Requirements for quality and competence
- ISO/IEC 17025:2005 General requirements for the competence of testing and calibration laboratories
- ISO 15190:2003 Medical laboratories – Requirements for safety
- ISO 19011:2011 Guidelines for auditing management systems

[1] http://www.bbmri-eric.eu/BBMRI-ERIC/quality-management/

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- Others to be examine more closely

Additional Guidelines, Best Practices and standards

- NFS 96-900 Certification des Centres de Resources Biologiques
- ISBER Best practices for Repositories

CEN/Technical Specifications for human specimen handling processes

Scope of the Technical Specifications: The Technical Specifications recommending the handling, documentation and processing of specimens intended for the analysis of the "specific scope of application" during the pre-analytical phase before a molecular assay is performed. The Technical Specifications are applicable to molecular in vitro diagnostic examinations (e.g., in vitro diagnostic laboratories, laboratory customers, in vitro diagnostics developers and manufacturers, institutions and commercial organisations performing biomedical research, **biobanks**, and regulatory authorities).

- Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for snap frozen tissue – Part 1: Isolated RNA, CEN/TS 16826-1
- Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for snap frozen tissue – Part 2: Isolated proteins, CEN/TS 16826-2
- Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for FFPE tissue – Part 1: Isolated RNA CEN/TS 16827-1
- Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for FFPE tissue – Part 2: Isolated proteins, CEN/TS 16827-2
- Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for FFPE tissue – Part 3: Isolated DNA, CEN/TS 16827-3
- Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood – Part 1: Isolated cellular RNA, CEN/TS 16835-1
- Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood – Part 2: Isolated genomic DNA CEN/TS 16835-2,
- Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood – Part 3: Isolated circ. cell-free DNA from plasma, CEN/TS 16835-3
- Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for metabolomics in urine, serum and plasma, CEN/TS 16945:2016

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Common Minimum Technical Standards and Protocols for Biobanks Dedicated to Cancer Research (IARC Technical Publications 2017)[2]
Scope: recommendations for biobanks not only in high-income countries but also in low- and middle-income countries (LMICs). The recommendations are based on validated and/or evidence-based guidelines. The book includes sections on sample sharing, ethical, legal, and social issues (ELSI), and harmonization guidelines important to support collaborative research efforts that make use of biological materials.

2.2 BBMRI-ERIC provides Self-Assessment Surveys[3]

BBMRI-ERIC provides Self-Assessment Surveys (BBMRI-ERIC SAS) based on the requirements of each of the nine existing CEN/TS. The surveys were created by transforming the sample handling procedure requirements described in the CEN/TS into a set of questions asking for the compliance in each handling step.

Together, the CEN/TS and the Self-Assessment Surveys provides a supplementary package for biobankers and researcher to control and assess the quality of human specimens.

2.3 Standardisation of generic Pre-analytical procedures for In-vitro DIAgnostics for Personalized Medicine – Link to SPIDIA4P

BBMRI-ERIC is partner of the H2020 Project SPIDIA4P[4] of which the objective is to develop new harmonized pan-European pre-analytical standards in cooperation with the European Committee for Standardization (CEN) and implemented in European countries for in vitro diagnostics in Personalized Medicine. These new standards will affect human specimen handling procedures from donor to laboratory applications.

- 4 new pre-analytical CEN/TS Documents for in venous whole blood circulating Tumour and Organ Cells (DNA, RNA, Proteins, staining procedures),
- 1 for Venous Whole Blood Exosomes / cell-free circulating RNA,
- 1 for Saliva (DNA),
- 1 for Frozen Tissues (DNA),
- 1 for Urine and other body fluids (cell-free DNA),
- 3 for Fine Needle Aspirates (RNA, DNA, Proteins),
- 1 for Saliva and Stool Microbiomes (DNA).

All standards will be in general applicable to human specimen handling procedures and to any kind of disease.

[2] http://publications.iarc.fr/551

[3] http://www.bbmri-eric.eu/services/self-assessment-survey/

[4] http://www.spidia.eu

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2.4 On-going work on quality of datasets – towards FAIR data

IT community of BBMRI-ERIC has developed an initial proposal for provenance information management, describing the whole chain from the research participant (consenting donor/patient) to biological samples to data generated and processed. This topic has been tentatively adopted by ISO TC276 Working Group 5 (WG5) and BBMRI-ERIC has submitted it as an official Preliminary Work Item in 2017 for voting by the ISO TC276. The standard is expected to be developed within the ISO WG5, aiming at improving reproducibility of medical research, which has become a major topic in the last decade. It will build in exisisting general provenance information standards such as W3C PROV and ISO

2.5 RD Standard Operating Procedures (SOPs) – link to the EuroBioBank network

The biobank should have adopted SOPs regulating:

- sample (and data) acquisition
- testing to ensure sample (and data) integrity
- sample processing and storage

Currently, a database on validated Standard Operating Procedures (SOPs) relevant in RD field exists at EuroBioBank database[5] providing SOPs for DNA extraction, muscle tissue processing, myoblast cell cultures, fibroblast cell cultures, lymphocyte and suspension cell line cultures, common aspects for human cell cultures as well as packaging and transport of biological resources. These are in compliance with OECD's recommendations for Biological Resource Centers.

[5] http://www.eurobiobank.org/biobanking-sops/

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3. Discussion and Conclusions

The use of best practices and quality standards in RD field is, similar to any other biobanking area, dependent of the sample type in question, data linked to it and the intended research use. Considering the preciousness due to their scarcity, it is if anything even more important to adhere to widely accepted quality standards to advance data reusablity. In the preceding paragraphs an overview has been given of an extensive set of quality assessment and management guidelines as currently developed internationally. The development of these guidelines has been guided by thorough validation and best practice development. This is far easier to do for common disese areas than for rare diseases, once again due to their relative scarcity, but also due to their heterogeneity, precluding large scale outcome comparisons.

Taking these considerations together, we conclude that in most cases the biobanking of RD samples and their pertaining data would do best to closely follow the existing and developing methodologies of the common disease field.

Not withstanding this, there will in applicable cases be RD-(sub)type-specific procedures which need to go well beyond the resolution and the practicable for common disease biobanking. To optimize these procedures, it seems best to develop RD specific refinements, which yield data formats interoperable with the common disease field.

4. Next Steps

BBMRI-ERIC will continue actively supporting Rare Disease biobanks with regards to building and improving their quality management systems with a specific focus on the pre-examination of sample processing. Future developments on the quality of samples and data for biobanks will also be continued providing a list of standards and SOPs relevant for the RD biobanks. BBMRI-ERIC has a key role in facilitating pan-European supply of good sample quality by operating as the information hub for the latest developments and supporting the implementation of the new quality standards within the biobanks in Europe.

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5. References

Biobanks Europe – Issue No. 6/2017

BBMRI-ERIC Annual and Financial Report 2016

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