ADOPT BBMRI-ERIC
GRANT AGREEMENT NO. 676550

ANNUAL REPORT

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1. Publishable Summary of ADOPT BBMRI-ERIC

BBMRI-ERIC: the Biobanking and BioMolecular resources Research Infrastructure - European Research Infrastructure Consortium, aims to establish, operate and develop a Pan-European distributed research infrastructure in order to facilitate the access to biological resources as well as facilities and to support high quality biomolecular and biomedical research. The ADOPT BBMRI-ERIC proposal aims at boosting and accelerating implementation of BBMRI-ERIC and its services. Its main deliverables are designed to complete or launch the construction of key Common Services of the Research Infrastructure as required for ESFRI-projects "under implementation", reflecting the targets of the European Research Area (ERA). One of the challenges in the post-genomic era is the research on common complex diseases, such as cancer, diabetes and Alzheimer's disease. Revealing these diseases will depend critically on the study of human biological samples and data from large numbers of patients and healthy individuals. The EU's ageing population is will result in an increase in many of those diseases and consequently an increased healthcare expenditure for senior citizens. BBMRI-ERIC is a specific European asset having become a fundamental component in addressing the ongoing and future requirements particularly of Europe's health service frameworks, including competitiveness and innovativeness of health-related industries. Its implementation is essential for the understanding of the diversity of human diseases, biological samples and corresponding data, which are required for the development of any new drug or diagnostic assay and are, therefore, critical for the advancement in health research, ultimately leading to personalised medicine. BBMRI-ERIC will provide a gateway access to the collections of the European research community, expertise and services building on the outcome of ADOPT BBMRI-ERIC. With the outcomes of ADOPT, BBMRI-ERIC is able to demonstrate the benefits of a distributed Research Infrastructure that is operational for the benefit of high-quality research, innovation and international collaboration. BBMRI-ERIC will provide a gateway access to the collections of the European research community, expertise and services building on the outcome of ADOPT BBMI-ERIC**.**

Specifically, ADOPT BBMRI-ERIC aims to:

1) Facilitate access to quality defined human disease relevant biological resources including associated data in an efficient, quality controlled and ethically and legally compliant manner: gathering a collection of data sets for samples from 10 000 patients of colorectal cancer;
2) Provision of IT-gateway to European biobanks: Consolidated registry of BBMRI-ERIC biobanks and the user interface for collection of colorectal cancer cases;
3) Implementation of harmonized access procedures in European biobanks;
4) Implementation of the essential ELSI tools for the users and enlarge Stakeholder involvement;
5) Development an integrated solution for biobanks to optimally meet user's needs in biomarker research, development and validation;
6) Establishment of a Common Service for Rare Diseases;
7) Identifying new Memberships/Observerships for BBMRI-ERIC and building cooperation with similar resources infrastructures to BBMRI-ERIC in North America and China, South America, the Gulf Region and Africa.

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Document log

Issue	Date	Comment	Author/partner
D1.1-Rev1	2017-08-16	Inclusion of EU funding recognition to comply with Grant Agreement art. 29.4. Updates on Deliverable Template.	Outi Törnwall

2. Description of the work performed and main results

Coordination

During the first year of ADOPT, the governance, coordination and communication activities have been carried out including administrative, financial, legal and technical work necessary for an efficient management and cooperation of the network. The first evaluation of the progress of ADOPT was completed in March 2016 by the International Advisory Committee (IAC) whose report addressed the existing/potential challenges and proposed recommendations for future actions. BBMRI-ERIC intranet has been used as a distribution and communication platform for information. In September 2016, BBMRI-ERIC launched a new website in order to better inform its members and community as a whole. Through this venue, the services, publications and topical news of BBMRI-ERIC are accessible to the wider audience. ADOPT project progress is reported yearly in the *Biobanks Europe* Magazine, the first report was published in the Issue No 4/2016.

Datasets – Organizing national biobanks and establishing what samples and data each Country can offer

The work towards mapping the available resources and defining the quality of samples in the national biobanks has been on-going in many levels. The parameters for measuring the quality level and richness in samples and data have been designed, and the questionnaire allowing the biobanks to describe themselves in terms of primacy, access, policy, data protection and management policy, informed consent, infrastructure and management, quality management and charges, has been piloted and validated. The work on collecting 10 000 colorectal cancer cases have been initiated by a survey through which the National Nodes have identified 60 relevant biobanks in Europe, eligible candidates for the colorectal cancer cohort collection. Further work involves the definition of the colorectal cancer data set that is to be collected with each cancer case.

IT Gateway to European biobanks

The Directory 2.0 was published first in December 2015 covering the description of biobank networks as oppose to the Directory 1.0 version. Currently, the consolidated registry of BBMRI-ERIC biobanks includes 515 biobanks and standalone collections. The work on the Directory resulted in a technical paper describing the Directory 2.0, which has been submitted for publication. During 2016, ADOPT BBMRI-ERIC reported on Security and Privacy Architecture, describing the risk analysis, architecture of BBMRI-ERIC IT services and how the security and privacy protection is build into them. As BBMRI-ERIC deals with human material and data, the privacy by design is paramount. Finally, ADOPT BBMRI-ERIC has created a data dictionary in relation to the colorectal cancer collection, which serves both as specification for the on-line portal system (for 3000 manually collected cases) and as the basis for a future ontology of colon cancer. The dictionary has been implemented for the set up of the on-line portal system, the software for entering data about colorectal cancer cases. With the on-line portal software, it is now possible to start gathering the data from different biobanks partaking the collection.

Access – Harmonized procedure and common principles to access samples harboured in BBMRI-ERIC biobanks

The principles pertaining to providing access to samples and data have been discussed and agreed upon with the BBMRI-ERIC National Node Directors. As a result, *Harmonised Access Procedure to Samples and Data*, a framework document that specifies the access criteria and procedures for requesting access to samples and data through BBMRI-ERIC, has been composed. The access is described step-by-step from registration to completion at the pan-European and national levels. The role of BBMRI-ERIC is to operate as a facilitator in the provision of access while the local biobanks stay in control of granting access based on their existing access policies, proper peer review and ethical assessment of research proposals.

ELSI and Stakeholder Forum

Several ELSI tools (*hSERN*: a tool for finding administrative and legal information for exchanges of human biological samples for research use in Europe; *legal WIKI*: a platform for sharing/discussing and validating reliable legal forms and standards; *Legal Assessment tool*: for raising awareness of formal requirements when sharing data) have been linked to the BBMRI-ERIC web in aims to implement the existing tools into a more user-friendly single tool. The public launch is forthcoming within 2017. ELSI work has progressed regarding the establishment of federated Helpdesk that will provide general information on topics that are curial for biobanking (e.g. informed consent, data protections and support on ethical questions). In August 2016, ELSI services were published in a flyer, functioning as a booklet describing the services of Common Service ELSI for its users. The service pricing of the services is currently under consideration after the fist exploration of bases for pricing webinar took place in May 2016. Two workshops have taken place in 2015 and 2016 in topics of 'Sharing and access to data and biospecimens for the benefit of patients', and 'Ethics Review of European Biobank Research', respectively. Finally, the draft framework on Ethical Governance and Ethics Check was presented in liaison with CORBEL project in March 2016.

BBMRI-ERIC has taken significant steps to involve the key stakeholders in its work to ensure that their voice is heard and represented in biomolecular and health research in Europe. Patent advocacy groups were met with in April 2016 and the stakeholder engagement was officially launched. The meeting marks the beginning of a transparent consultation and participatory stakeholder engagement process, which will be enlarged by additional chapters involving industry and learned societies representatives at a later stages.

Biomarker: Translation to Medicine

Progress in advancing the compliance with the CEN (European Committee for Standardization) norms has materialised into a prototype of a Self-Assessment Tool for CEN conformity. This tool is an excel based checklist that provides the biobanks a way to evaluate how well their processes are in compliance with the CEN Technical Specifications. It will also provide a supportive instrument to crosscheck the current Standard Operating Procedures and to adapt these according to the CEN specifications. The Online Self-Assessment tool will be launched during the first quarter of 2017.

BBMRI-ERIC has developed a plan how to become a BBMRI-ERIC Expert Centre – trusted partner. In June 2016, CBmed became the first BBMRI-ERIC Expert Centre with a special emphasis in identifying new biomarkers, validating potential biomarkers and conducting translational biomarker research for products to be used in the clinical practice. The design of the Expert Centre model allows improved access to biobanks for industry, and particularly with the colorectal cancer cohort collection it can result in series of biomarker programmes in the

field of precision medicine providing an example not only for colorectal cancer but also for essentially all disease fields.

Common Service for Rare Diseases

Helpdesk application was installed in mid 2016 enabling real-time support for Rare Disease (RD) biobanks and or registries. The application allows users from both inside and outside of BBMRI-ERIC to submit requests/questions and assigns these requests to the responsible people and monitors their progress to the completion. A background document describing the Helpdesk models and level of support has also been developed to facilitate the implementation of the helpdesk functions.

The coordination and integration of existing RD biobanks and resources and the development of further expertise have materialized in biobanking activities within the RD community. Networking meetings have taken place with RD-CONNECT, EuroBioBank and ECRD as well as within the ERN Framework.

Internationalisation

Several approaches to link-up the scientists and networks from different regions of the globe have been made during face-to-face meetings and workshops (UN, Africa and China, EUROMED and BBMRI-LPC Forum). Whereas most of the work for connecting networks has so far done in Europe, the future focus of the ADOPT will be for other regions as well.

The first concrete result of the Memorandum of Understanding with P3G was t
The joint efforts to organise the 2016 Europe Biobank Week together with ESBB, P3G and BBMRI-LPC. Within the Europe Biobank Week (BBMRI-LPC Forum), a report on country mapping efforts was delivered in which prospective new member countries for BBMRI-ERIC were identified.

ADOPT Project meeting in Malta, May 2016.

3. Deliverables and milestones

WP1

Del.no.	Deliverable name	WP no.	Nature	Dissemination level	Delivery date	Status
D1.1	Setup of all bodies like the international Advisory Committee, etc.	**1**	OTHER	PU	**M1**	✔
D1.2	Release of the project specific website, and adaption of the internal communication platform and mailing lists	**1**	DEC	PU	**M2**	✔
D1.3	Implementation of performance, outcome and impact indicators	**1**	R	PU	**M12**	✔
D1.4	General annual reports	**1**	OTHER	PU	**M13, 25**	M13 ✔
D1.5	Reports of the Advisory Committee meetings	**1**	R	PU	**M7, 19**	M7 ✔
D1.6	Final report	**1**	OTHER	PU	**M36**	
Milestone			**Means of verification**			**Status**
MS1	Kick-off Meeting		Kick-off Meeting			✔
MS2	Publishes Survey of BBMRI-ERIC performance indicators		Publishes Survey of BBMRI-ERIC performance indicators		**M36**	

WP2

Del.no.	Deliverable name	WP	Nature	Dissemination level	Delivery date	Status
D2.1	Procedure and checklist on on-site visit evaluation	**2**	R	PU	**M8**	✔
D2.2	List of qualified EU biobanks	**2**	R	PU	**M9**	✔
D2.3	List of data, services technologies/technologic platforms for each Country	**2**	R	PU	**M9**	***DELAYED,*** *will be delivered in conjunction with WP6 work D6.4.*
D2.4	Data set on samples from colorectal cancer patients	**2**	OTHER	PU	**M24**	
D2.5	Data matrix for characterisation of diseases	**2**	R	PU	**M24**	
D2.6	Performance indicators for biobanks	**2**	R	PU	**M24**	
D2.7	Patient-related data for colorectal cancer samples	**2**	R	PU	**M36**	
Milestone			**Means of verification**			**Status**
MS3	Implementation of procedures for evaluation of biobanks		Implementation of procedures for biobanks evaluation		**M12**	*Pilot BBMRI.it* ✔

MS4	Cohort of 10 000 cases of colon cancer patients' samples and data		Cohort of 10 000 cases of colon cancer patients samples and data		**M30**	
MS5	Performance indicators for biobanks monitored in all Member States		Performance indicators for biobanks monitored in all Member States		**M36**	

WP3

Del.no.	**Deliverable name**	**WP**	**Nature**	**Dissemination level**	**Delivery date**	**Status**
D3.1	Consolidated registry of BBMRI-ERIC biobanks (task 1, lead UMCG)	**3**	OTHER	PU	**M12**	✔
D3.2	Security and privacy architecture (task 2, lead DKFZ)	**3**	R	PU	**M12**	✔
D3.3	User interfase for collection of the colon cancer cases and database (task 3, lead FAU)	**3**	OTHER	PU	**M12**	✔
D3.4	Implementation of the BBMRI-ERIC architecture and database	**3**	OTHER	PU	**M12, M36**	M12 ✔
D3.5	Ontology-based toolset for mapping of the biobanking terminologies	**3**	OTHER	PU	**M18, M30**	
D3.6	Biobank connector specification and reference connector implementation	**3**	OTHER	PU	**M18**	
Milestone			**Means of verification**			**Status**
M3.1/MS6	Deployment of the consolidated registry of BBMRI-ERIC biobanks		Consolidated Registry		**M3**	✔
M3.2/MS 7	Deployment of the first version of BBMRI-ERIC hub infrastructure		Hub infrastructure		**M18**	

WP4

Del.no.	**Deliverable name**	**WP**	**Nature**	**Dissemination level**	**Delivery date**	**Status**
D4.1	Harmonised access procedure to samples and data	**4**	R	PU	**M12**	✔
D4.2	Report on harmonised cost recovery process	**4**	R	PU	**M24**	
D4.3	Report on return to investment models	**4**	R	PU	**M24**	
D4.4	Reports on the access procedure	**4**	R	PU	**M24, M36**	
Milestone			**Means of verification**			**Status**
MS8	Operational access procedure of BBMRI-ERIC		Operational access procedure		**M12**	✔

MS9	Harmonised cost recovery process		Harmonised cost recovery process		**M24**	
MS10	Performance indicators for access monitored in all Member States		Performance indicators for access monitored in all Member States		**M36**	

WP5

Del.no.	Deliverable name	WP	Nature	Dissemination level	Delivery date	Status
D4.5	Implementation of new ELSI tools, notably procedure to enhance public debate	**4**	OTHER	PU	**M12, M36**	✔
D5.1	Booklet describing processes and tools in place for the operation of the Common Service ELSI for its users	**5**	R	PU	**M6, M24, M36**	M6 ✔
D5.2	Annual workshops & reports and possible consensus statements on specific topics.	**5**	OTHER	PU	**M12, M24**	M12 ✔
D5.3	Operational platform for sharing experience: Meeting with representatives of national/regional ethics committees	**5**	OTHER	PU	**M24**	
D5.4	Formal certification according to relevant standards	**5**	OTHER	PU	**M30**	
D5.5	Report on educational and training events and tools	**5**	R	PU	**M36**	
D5.6	Stakeholder Forum Meeting Report	**5**	R	PU	**M12, M24**	M12 ✔
D5.7	Ethical Governance Framework and ethics check for ADOPT BBMRI-ERIC	**6**	OTHER	PU	**M6**	✔
Milestone						
MS11	Existing ELSI tools implemented accordingly		Existing ELSI tools implemented accordingly		**M6**	✔
MS12	New ELSI tools identified		New ELSI tools identified		**M8**	✔
MS13	Stakeholder Forum Meeting		Two meetings (1st M10, 2nd M22)		**M10, M22**	M10 ✔

WP6

Del.no.	Deliverable name	WP	Nature	Dissemination level	Delivery date	Status
D6.1	Guideline for biobanks to comply with EU in vitro diagnostics regulation	**6**	R	PU	**M18**	
D6.2	Handbook for user needs	**6**	Websites, patents etc.	PU	**M36**	
D6.3	IT-tool for monitoring compliance of biobanks with CENT TS for molecular diagnostics examination	**6**	OTHER	PU	**M18**	

D6.4	Best practice document for optimal usage of omics technologies for biomarkers	**6**	R	PU	**M24**	
D6.5	Letter of Interest of founding members of a Biomarker Expert Centre	**6**	OTHER	PU	**M36**	
D6.6	Collaboration agreement with other ESFRI-BMS Ris, IMI and national biomarker programmes	**6**	OTHER	PU	**M36**	
Milestone			Means of verification			**Status**
MS14	Guideline for biobanks to comply with EU in vitro diagnostics regulations published		Guideline for biobanks to comply with EU in vitro diagnostics regulations published		**M24**	
MS15	CEN TS compliance of biobanks monitored and reported by BBMRI-ERIC		CEN TS compliance of biobanks monitored and reported by BBMRI-ERIC		**M24**	
MS16	Plan for a new biomarker programme with other ESFRI-MBS infrastructures, IMI or National biomarker programmes		Plan for a new biomarker programme with other ESFRI-MBS infrastructures, IMI or National biomarker programmes		**M36**	

WP7

Del.no.	**Deliverable name**	**WP**	**Nature**	**Dissemination level**	**Delivery date**	**Status**
D7.1	Reports from meetings of the coordination activity	**7**	R	PU	**M12, M24, M36**	M12 ✔
D7.2	Registry/biobank support service/ Help-desk facility	**7**	OTHER	PU	**M12**	✔
D7.3	Harmonised quality standards	**7**	R	PU	**M24**	
D7.4	Governance model for the sustainability of RD biobanks	**7**	R	PU	**M24**	
D7.5	RD Biobank section in BBMRI- ERIC catalogue	**7**	OTHER	PU	**M18**	
D7.6	Report of the Pilot Study	**7**	R	PU	**M36**	
D7.7	Implementation of the RD Common Service	**7**	OTHER	PU	**M36**	
Milestone			**Means of verification**			**Status**
MS17	ID Card for RD biobanks		ID Card for RD biobanks		**M12**	✔
MS18	Implementation of harmonized quality standards in the Osteogenesis Imperfecta pilot		Implementation of harmonized quality standards in the Osteogenesis Imperfecta pilot		**M24**	
MS19	Receipt of the first RD-Helpdesk request		Receipt of the first RD-Helpdesk request		**M30**	
MS20	Fulfillment of the first RD Helpdesk request		Fulfillment of the first RD Helpdesk request		**M36**	

WP8

Del.no.	Deliverable name	WP	Nature	Dissemination level	Delivery date	Status
D8.1	Report of country mapping in the field of biobanking	**8**	R	PU	**M12**	✔
D8.2	Workshops held within the 4 regions of primary interest	**8**	Websites patents, etc.	PU	**M6, M12, M24, M36**	M 6, 12 ✔
D8.3	Final report of WP8	**8**	R	PU	**M36**	
Milestone						**Status**
M8.1	MoU signed with P3G, the African Union, the United Arab Emirates, and China		MoU signed with P3G, the African Union, the United Arab Emirates, and China		**First one M6**	P3G ✔
M8.2	3 new BBMRI-ERIC Members/Observers		3 new BBMRI-ERIC Members/Observers		**M18**	
M8.3	2 new BBMRI-ERIC Members/Observers		2 new BBMRI-ERIC Members/Observers		**M36**	

4. Detailed reports from Work Packages

WP1 – Coordination and Project Management

Work Package leader: Jan-Eric Litton, BBMRI-ERIC

Project Manager: Outi Törnwall, BBMRI-ERIC

Task 1 - Work Package management (lead: BBMRI-ERIC):

The management activities by the BBMRI-ERIC Headquaters have included monitoring and reporting of the progress of the work and tasks. Regular bi-monthly meetings have been organized and the project progress is monitored twice a year.

Task 2 and 3 – Governance (lead: BBMRI-ERIC):

WP1 has set up the governance structure to follow that of the BBMRI-ERIC. The International Advisory Committee (IAC) is the only external governance body that was set up specifically for ADOPT. IAC meeting was held in March 2016 for the evaluation of ADOPT and a report on the project progress was published in April 2016. The WP1 has worked on communication by using the internal (intranet, e-mail lists) and eternal (webpage, Biobanks Magazine, external meetings) communication channels of BBMRI-ERIC.

Task 4 - Evaluation of Implemented Governance (lead: BBMRI-ERIC):

BBMRI-ERIC has established and published a proposed set of Performance Indicators serving as tools to monitor the operation of the infrastructure in multiple levels (Pan-European, National Node and biobank level). A subset of Performance Indicators has been proposed as future BBMRI-ERIC Key Performance Indicators. The consensus on the subset is to be reached in 2017.

WP2 – Data sets

Work Package leader: Marialuisa Lavitrano, BBMRI.it

Co-leader: Georges Dagher[1], BBMRI.fr

Task 1 - Mapping and selection of well-established EU biobanks, complying with the BBMRI-ERIC procedures (lead: BBMRI.it):

Self-Assessment tool: The parameters for measuring the quality level and richness of samples and data in the European biobanks have been defined by the WP2 working group. The Self Assessment Tool is built up on the needs of biobankers, and takes into account the Quality Management System in general, pre-examination processes and performance evaluation (Product specification report). The results are also reported to the Work Stream 2 Quality of the 2016 Work Programme of BBMRI-ERIC, Work Stream 2.1: Molecular In-vitro Diagnostic Examination of CEN/TC and Work Stream 2.2 Self Assessment Tool for Biobanks (BBMRI-ERIC Work Programme 2016).

The work takes into account the documents and guidelines, specifically referred to, in the BBMRI-ERIC Partner Charter (OECD best practice guidelines for Biological Resource Centres and WHO/IARC guidelines for biological resource centres for cancer research), and additional National and International Guidelines

(NFS 96-900 Certification des Centres de Resources Biologiques, ISBER Best practices for Repositories, ISO 9001:2015 Quality management systems requirements, ISO 15189:2012 Medical laboratories – Requirements for quality and competence, ISO 17025:2005 General requirements for the competence of testing and calibration laboratories, ISO 19011:2011 Guidelines for auditing management systems). All parameters for compliance with the BBMRI-ERIC Partner Charter have been applied: primacy, access policy, data protection and management policy, informed consent, infrastructure and management, quality management, charges.

Questionnaire and Pre-An Tool: Already available tools produced by the Italian Node (questionnaire BBMRI.it) and by the Austrian Node (Pre-An Tool) were analysed, with the aim of a) building a self-evaluation questionnaire, taking into account all parameters relevant to the quality management of biobanks; b) defining a standardized method of evaluation, by giving a score to each parameter and by weighing the items under evaluation on the basis of their respective importance; c) providing the self-evaluation tool to the National Nodes, in order to adapt it to specific requirements; d) assessing the efficacy of this evaluation system through on-site audits of biobanks.

The criteria defined by the Parameters subgroup of the BioResource Impact Factor (BRIF) initiative (1) have also been taken into account in designing the questionnaire and in defining the method of evaluation. Scores and sub-scores have been defined for seven features of the biobanks: quality, transparency, catalogue, usage, connectivity, innovation and scientific production, sustainability and impact. For each item sub scores have also been set and weighted. Quality includes 8 sub-scores (QMS, certification, QC/proficiency testing, SOPs, plan of improvements, staff competence, Regular audits/inspections, disaster recovery plan), Transparency includes 5 sub-scores (web site, annual report, access/prioritization policy, donors' information and consent, involvement of donors/public); Catalogue includes 4 sub-scores (diffusion modality, sample variability, sample number, data availability); Usage includes 5 sub-scores (reality of supply, sharing procedure, numbers of requests, Material Transfer Agreement, ratio collected/used material); Connectivity includes 3 sub-scores (thematic network participation, regional network participation, infrastructure participation); Innovation and Scientific Production include 3 sub-scores (publications traceability, authorship and acknowledgements, data recovery); Sustainability and Impact include 5 sub-scores (institutional recognition, medium and long-term funding, grants obtained, cost recovery, dedicated staff). As to the pre-analytical self-evaluation tool, it is based upon the Molecular In-vitro Diagnostic Examination of CEN/TC, it is available on-line and it is being validated by the Austrian National Node.

The Italian Node has produced and validated the BBMRI.it questionnaire, the grid for the biobank assessment, the path for membership and procedure and check lists for site visits/audits, the French Node has outlined the parameters for measuring quality and use of the biobanks, and the Austrian Node has produced the pre-analytical tool. All products have been validated by the respective National biobanks. The other Nodes involved in WP2 are validating the tools within the respective National biobanks.

The parameters are built in order to: a) identify biobanks who give assurance of service to the scientific community, interoperability, compliance with ethical and legal standards, compliance with National and International best practices; b) help biobanks and their host institutions in identifying strengths and weaknesses in their Quality System; c) help National Nodes to develop services and tools for improving quality and efficiency of their networks; d) support the Member States in allocating financial resources to improve quality of biobanking; e) sustain the construction of a European biobank network working under common and agreed standards, compatible with signing the Partner Charter of BBMRI-ERIC; f) collaborate with international initiatives.

The list of qualified EU biobanks was established in M8 consisting of 60 relevant biobanks in Europe. Biobanks included in the list are the ones willing to collaborate in the context of ADOPT project at this point. The mapping of biobanks and qualification criteria will be updated continuously throughout the project.

Task 1.2. Validation of information provided under Task 1.1 through peer-review on-site visits of biobanks by experts in the field (lead: BBMRI.it):

BBMRI.it has designed a path for membership of biobanks. The strategy was initially based on direct contact and then on the use of a communication platform. The path to membership of biobanks in BBMRI.it takes place in three phases. *First phase: Survey*. a survey of the Italian biobanks was made, with the aim to map and select the best-known Italian biobanks and stratify based on the level of quality and richness of associated samples and data. *Second phase: Assessment*, aimed at identifying the "real" biobanks and distinguish them from facilities just holding collections of samples. To this end, BBMRI.it has proposed to the biobanks an on-line self-assessment questionnaire. More than ninety biobanks have completed the questionnaire and responses were evaluated by an ad hoc committee, using as reference the quality and ELSI requirements defined in the BBMRI-ERIC partner charter: access to samples, data protection policy, informed consent, infrastructure, quality system. The purpose of the evaluation is a) to verify the compliance of biobanks with BBMRI-ERIC requirements, and b) to identify the strengths and needs of biobanks and collections, in order to make available adequate support services to the network. Each biobank has been examined by at least three evaluators, and each of them has assigned a score to each of the elements considered on the basis of a defined score system. The biobank managers were then contacted directly, in order to better analyse strengths and weaknesses detected by the evaluators.

Check lists and procedures for site visits have been set up aimed to standardise the checklist containing the set of questions/topics to be covered during the on-site visit, and site visits and audits were carried out for 10 national biobanks and are foreseen for all biobanks belonging to the National network. This process has allowed the Node to have a more accurate picture of the national scene and to create a direct contact with biobanks. The great majority of biobanks have already been shown to operate in accordance with the principles of BBMRI-ERIC. The other biobanks willing to complete the compliance path receive the support of the National Node through the Common Services. *Third phase: Signing the BBMRI-ERIC Partner Charter.* Each Biobank/Biological Resource Centre, which operates in accordance with national and international good practices, through the signing of the Partner Charter becomes full member of BBMRI.it and consequently enters the European infrastructure BBMRI-ERIC. A biobank web page is designed by the IT common services and the Directors become member of the Board of Directors of BBMRI.it. To date, the legal representatives of 33 biobanks have signed the Partner Charter. The path of joining the network designed by BBMRI.it has been adopted by BBMRI-ERIC as a pilot for the assessment of biobanks at the European level. The National Nodes involved in WP2 will validate the checklists and procedures for site visits produced and will apply them to the respective biobanks.

Task 1.3. Establish what each National Node will precisely offer in terms of samples and data (lead: BBMRI.it):

Validated accessibility of samples and data to address needs of precision medicine in colorectal cancer is the goal of WP2, and samples (e.g., tissues [fresh frozen or FFPE; cancer and normal tissue], serum, plasma, fcDNA, cells) and associated data of 10,000 patients from all BBMRI-ERIC Members will be collected (~3,000 manually collected plus 7,000 based on BBMRI gateway for automated data gathering realized in WP3). The dataset associated with colorectal cancer samples to be collected was originally described in the ADOPT WP2 description. Now, the dataset has been analysed within the working group to define the *final data set* to be collected as a part of ADOPT BBMRI-ERIC project. The development is done in several steps:

- Basic consensus on collected attributes among the medical experts,
- Development of formal model including entities, their attributes and their mutual relations by IT experts,
- Review of the formal model by the joint group of medical and IT experts,
- Approval of the resulting formal model by the BBMRI-ERIC Management Committee (used also as project management board in ADOPT BBMRI-ERIC project),
- Development of the data collection application (ADOPT WP3) for manual data collection (manual data collection itself will be done within ADOPT WP2).

A consensus has been reached on the inclusion criteria (not directly part of the data model, but also necessary for correct interpretation of the resulting data set): Colorectal cancer as a primary diagnosis, Available FFPE – surgical material, Availability of all REQUIRED data, Willingness to provide access to (a) samples, (b) pseudonymized data as a part of (i) participation in research projects, (ii) cost or no-cost recovery procedure. This assumes signing MTA/DTA.

To acquire information about services and specific technologies/technological platforms at each National Node, a questionnaire has been set up in collaboration with WP6. The questionnaire will be sent to National Node directors to collect data on Analysis Service Platforms used for: GWAS, WGS, WES, metabolomics, proteomics, transcriptomics, epigenomics and access procedures

The task to establish what each National Node will precisely offer in terms of samples and data to European Biobanks is performed together with WP3 IT-Gateway, by an interdisciplinary group including biobankers, clinicians, disease registry experts, researchers, IT experts. The task to acquire information about services and specific technologies/technological platforms at each National Node is performed together with WP6.

Task 2 – Validated accessibility of samples and data to address needs of precision medicine in colorectal cancer (lead: BBMRI.it):

Well-characterised human samples and associated data are unique resources for identification of new molecular features to be used as diagnostic and/or therapeutic targets. Samples have to comply with international quality standards (Task 3 WP6). The European Committee for Standardization (CEN) recently published Technical Specifications on “Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for different sample types”. These Technical Specifications (CEN/TS) serve as basis for evaluating the performance, quality, and comparability of European biobanks. The -BBMRI-ERIC quality working group is reviewing the CEN/TS with regard to the applicability for European biobanks, focusing on the pre-analytical phase for: a) formalin-fixed and paraffin-embedded (FFPE) tissue specimens intended for DNA, RNA, and protein analysis; b) venous whole blood; c) snap frozen tissue: Isolated RNA and proteins.

Task 3 – Collection of data sets for samples from colorectal cancer patients (lead: BBMRI.it):

The data should be provided in a standardised format as defined in WP3. The collection will therefore start with the manual process, and as soon as the IT tool for semi-automated data gathering is provided by WP3.

A CONSENSUS HAS BEEN REACHED ON THE DEFINITION OF THE DATA SET ITEMS. ALL THE PROPERTIES THAT ARE NECESSARY FOR UNAMBIGUOUS INTERPRETATION OF THE RESULTS HAVE BEEN DEFINED. THIS INCLUDES THE FOLLOWING PROPERTIES FOR EACH COLLECTED VARIABLE (ATTRIBUTE):

- Unique label of the variable
- Short description (label) of the variable - to be used in forms.
- Semantics = definition of meaning
    - This includes references to existing clearly defined official standards or community "standards", including existing ontologies
    - We will use this for ontologizing the data model, in order to make it "machine readable" (allowing for correct interpretation of the data in automated processing workflows)
- Syntax
    - including data type (elementary types such as boolean, float, integer, free text, specifically structured text, etc., array or lists of elementary types)
    - including coding (e.g., IEEE 754 for floats, regular expressions for structured text)
- List of allowed units
    - including their conversion algorithms (with "non-existent" and "unknown" interim options)
- Level: REQUIRED, OPTIONAL, RECOMMENDED
    - REQUIRED means the data can't be entered at all without this item being provided
    - OPTIONAL means data may or may not be provided, but the item will be ready for inputting the data in as part of the data model
    - RECOMMENDED is a special subclass of the OPTIONAL, which is highly-recommended to be filled in (intended for items where we need the data but where we know that some sources won't be able to fill this in and we still want such data not being discarded as invalid).
- Relation to entities (patient, examination, etc.) - will be used for developing the formal model

Each single item of the dataset is identified based upon the criteria defined. The goal is to provide a detailed description of the data structure in order to (a) create useful data set for the colon cancer research, (b) allow for unambiguous interpretation of the data when used in the research.

WP3 – IT Gateway to European Biobanks

Work Package leader: Michael Hummel, BBMRI.de
Co-leader: Andres Metspalu, BBMRI.ee

Task 1 – Deployment and development of the BBMRI-ERIC Biobank Registry (lead: UMCG):

The Directory 2.0 has been developed during the M1-3 of ADOPT, delivering the first Milestone M3.1. This utilized Directory 1.0 previously released by BBMRI-ERIC, while bringing in fundamental changes in the data model to make it MIABIS 2.0 compliant, and to describe biobank networks (currently not covered by MIABIS 2.0), and updated implementation of the web interface for non-IT users. Preparation of Deliverable D3.1 has started after this milestone, resulting also in a technical paper describing Directory 2.0, which has been prepared for journal submission. Curation of data in the Directory 2.0 was a major task in order to make the data useful for the users.

Task 2 – Architectural Design and stepwise Implementation of a European Database for BBMRI-ERIC (lead: DKFZ):

A series of webinars were organized in order to map existing services related to Directory, Locator and Negotiator, developed and/or deployed at BBMRI-ERIC national nodes, as well as outside of BBMRI-ERIC community. First steps toward design have been taken in the beginning of 2016, defining use cases for the Negotiator and Locator services. At this time, the privacy architecture has been documented, including a detailed modeling of the services and message sequence charts. Moreover, with the delivery of the BBMRI-ERIC CS-IT architecture notebook, the Connector specification and its integration with the other services have been documented.

Task 3 Provide a Terminology Service for semantic ontology mapping (lead: FAU):

This task addresses the issue of semantic interoperability between data sources that always needs to be tackled, when data sharing between originally independent data sources even across Country borders shall be achieved. A series of webinars organized in the beginning of 2016 supported the analysis of existing data mapping services deployed at BBMRI-ERIC national nodes, as well as outside of BBMRI-ERIC community. The BBMRI-ERIC CS-IT architecture has been defined in detail in a report delivered on M12 – D3.3 "Implementation of the BBMRI-ERIC architecture and database". D3.2, the "User interface for collection of the colon cancer cases and database" has also been officially delivered. The integration between the Metadata Repository (MDR) and the user interface to manually enter data, for the BBMRI-ERIC colon cancer data collection, is in place.

Task 5 – Collection of colon cancer cases and their clinical data (lead: BBMRI.de):

WP3 worked closely with WP2 on defining the data model and exact attributes to be collected for the colon cancer cases. This data model served as an input to the data collection application, for the manual entry of 3.000 colon cancer cases. The data items are defined in the Metadata Repository (MDR).

WP4 – Access

Work Package leader: Georges Dagher[1], BBMRI.fr

Co-lead Marialuisa Lavitrano, BBMRI.it

[1] The Directrice adjointe, Frédérique Bulle, has informed BBMRI-ERIC that BBMRI.fr is taking new strategic directions. A new National Node Director will be nominated at a later stage, hence it is unclear who will continue George Dagher's work in ADOPT.

Task 1 – Implement in biobanks a harmonised procedure to access (lead: BBMRI-ERIC):

BBMRI-ERIC national coordinators discussed and agreed on the principles pertaining to providing access to samples and data. As a result, *Harmonised Access Procedure to Samples and Data*, a framework document, which specifies the access criteria and procedures for requesting access to samples and data through BBMRI-ERIC, has been composed. The access is described step-by-step from registration to completion at the pan-European and national levels. These principles described in the framework will govern the access to samples and data received by the BBMRI-ERIC Headquaters and National Nodes of BBMRI-ERIC. National coordinators will inform the biobank members of the national infrastructure about the access principles and procedures.

The access procedure includes 5 steps: Registration, request of samples and data, access control and sample/data delivery, return of results, request completion notification. The details of each step was discussed and agreed upon by BBMRI-ERIC national coordinators. The details pertaining to the characteristics of the requested samples and data were defined and agreed upon.

Common Service IT currently implements the request procedure, including the details concerning the sample and data characteristics, in a digital format. This web based access facilitator is expected to be available to researchers and biobanks before the end of December 2016.

WP5 – ELSI and Stakeholder Forum

Work Package leader: Anne Cambon-Thomsen, BBMRI-ERIC

Task 1 – Enlarge Stakeholder Involvement through Stakeholder Forum Meetings (lead: BBMRI-ERIC):

In its mission to facilitate the access to resources and support high quality biomolecular and medical research, BBMRI-ERIC aims to involve key stakeholders in its work to ensure their voice is heard and represented in European biomolecular and health research. As donations of valuable human biological samples and the corresponding data, stored by the biobanks, are essential for understanding human diseases and corresponding prevention programmes, BBMRI-ERIC is dedicated to consulting the biobanking stakeholder community in this process. Identifying patients as the most crucial stakeholder group, BBMRI-ERIC firstly met with representatives of patient advocacy groups representing areas of expertise on genetics, rare diseases, chronic diseases, healthy ageing/prevention, degenerative diseases, cancer, obesity, and infectious diseases on 19 April 2016, therewith re-launching its stakeholder engagement. The stakeholders of patient groups included BBMRI-ERIC, the European Institute of Women's Health, European Cancer Patient Coalition, EURORDIS - Rare Diseases Europe, Genetic Alliance UK, Altzheimer Europe, and the Dutch VSOP.

Patients and families with life limiting conditions do believe in the crucial role of scientific research to make new and better treatment available. Patients therefore accept to donate their data and samples to be shared amongst legitimate users for the purpose of advancing understanding and contributing to the realisation of the potential for health gain providing there is an appropriate framework in place. For these reasons, the patient stakeholder group believes it would be appropriate to establish a framework to support legitimate uses of data and samples, and reduce the risk of misuse or abuse of patient data to an acceptable level, bearing in mind that the elimination of all risk of misuse will probably only be achievable through the creation of a governance framework that is so tight that desirable applications are likely to be impeded to an unacceptable extent.

The meeting, chaired by Alastair Kent of Genetic Alliance UK, marked the beginning of a transparent consultation and participatory stakeholder engagement process, which will be enlarged by chapters on industry representatives and other organisations and learned societies (e.g., EFPIA, EMA, etc.). The overall aim is to address key issues for a continuous constructive dialogue to ensure stakeholders' needs are well represented in the activities of BBMRI-ERIC. As outlined in BBMRI-ERIC's Work Programme, the Stakeholder Forum is designed as a timely and dynamic platform of exchange building on participatory governance. The thematic topics in question will determine if one, some or all organisational chapters of the Stakeholder Forum will meet in smaller, topic-specific workshops. In 2016, the focus was on setting up the patient chapter. The interest of industry and learned societies was explored and allowed the launch of these respective chapters in 2017. The chairperson of the Stakeholder Forum shall be a patient advocacy group representative and by this function by default a member of the BBMRI-ERIC Scientific and Ethical Advisory Board.

Task 2 – Communication (lead: BBMRI-ERIC):

BBMRI-ERIC provides tools and expertise, as well as knowledge and experience sharing on ethical, legal and societal issues for the biobanking community through its Common Service ELSI. *Who is this service for?* The service offers support on ethical, legal and societal issues related to biobanking activities. It is primarily intended for users located in Member Countries of BBMRI-ERIC. In 2016, a flyer[1] has been developed to serve as the beta version for a more detailed booklet describing each process and tools in detail. A first exploration of bases for pricing the services was done through a webinar about experiences in some NN ELSI services (30/5/2016).

BBMRI-ERIC and its ELSI team have organized and held several (virtual and physical) working meetings as well as 2 Workshops; respectively the "Ethics Review of European Biobank Research: Towards Mutual Recognition?" Workshop (2016)[2] and the "Sharing and access to data and human biospecimens for the benefit of patients - Towards a BBMRI-ERIC Policy" Workshop (2015)[3].

All tools developed have to be challenged by the user feedback and constantly approved. Showcasing the tools during conferences (e.g. Europe Biobank Week) proved to be more successfull than dissemination via the e-newsflash as it provides a direct hands-on experience. Hence, marketing the tools via the Booklet and Flyer during conferences is key.

Task 3 – Piloting well-established Common Service ELSI tools (lead: BBMRI-ERIC):

Existing ELSI tools[4],[5],[6] have been incorporated/linked to the web (www.bbmri-eric.eu). The web domain, where hSERN is hosted, is owned by BBMRI-ERIC. The legal WIKI is hosted by BBMRI.se. In the context of this project and in liaison with the H2020 project CORBEL, we implement (parts of) the existing tools into a single, user-friendlier tool, therewith better addressing the user needs for practical legal guidance.

Task 4 – Common Service ELSI implementation of new developments (lead: BBMRI-ERIC):

The integration is on-going in a restricted web area (intranet, ELSI playground) and the single ELSI tool should be publicly launched 2016/2017. Moreover, the need for an ELSI helpdesk became apparent. Among other things, the ELSI-group is offering practical interpretation on new legislation. It also monitors relevant ethical and legal frameworks in development and communicates publications, research results, surveys, and informs about relevant meetings. We are also setting up a federated Helpdesk.[7] The vision and aim is to make the Helpdesk available, feasible, practical, usable, reliable, verifiable and sustainable. This Helpdesk will provide general information on topics that are crucial for biobanking, regarding for example informed consent, data protection and support on ethical questions. It will also offer customised help. The practical tools to help provide this service are currently under development together with IT experts.

The aim of this Ethical Governance Framework is to enable future members of BBMRI-ERIC to operate within agreed terms with respect to the participant consent, ethics committee approvals and national regulations, ensuring researchers supply and access data whilst working under a common ethical framework. The draft framework presented was written on the basis of other EU funded projects[8] and in liaison with CORBEL[9]. This,

[1] BBMRI-ERIC Common Service ELSI Flyer http://www.bbmri-eric.eu/wp-content/uploads/2016/08/BBMRI-ERIC_ELSI_Services_final.pdf
[2] Draft report, see Deliverable D5.2 Report as submitted.
[3] http://rubikon-web4.at/bbmri-eric/wp-content/uploads/2016/08/BBMRI-Paris-2015-ELSI-WORKSHOP-REPORT.pdf
[4] Wiki Legal, http://www.bbmri-wp4.eu/wiki/index.php/Main_Page
[5] Legal Assesment Tool, http://hhu2.at.xencon.de:8080/lat/
[6] hSERN, http://www.hsern.eu/
[7] http://www.bbmri-eric.eu/services/elsihelpdesk/
[8] Namely the BioMedBridges - FP7 Project GA n°284209 Deliverable on BioMedBridges Ethical Governance Framework ; CAGEKID, Cancer Genomics of the Kidney - FP7 Project GA n° 241669 , Deliverable 8.4; ESGI, European Sequencing and Genomics Infrastructure - FP7 Project GA n°262055, Deliverable 7.5 and 7.7.

in order to ensure reliability and consistency of the systems in place. Especially, the ethics check will be field-tested in the context of the colon cancer case study of ADOPT BBMRI-ERIC. This may lead to adaptions in the suggested framework prior to implementation within the research infrastructure BBMRI-ERIC, as agreed by the steering committee [NN directors of BBMRI-ERIC].

WP6 – Biomarker: Translation to Medicine

Work Package leader: Kurt Zatloukal, BBMRI.at

Co-leader: Anu Jalanko, BBMRI.fi

Task 1: Requirements on biobank design to optimally support biomarker discovery, development and validation (lead: BBMRI.fi):

The goal is to provide requirements on biobank design to support biomarker discovery, development and validation. The aim is to produce a publication reviewing existing guidance in BBMRI-ERIC member countries. BBMRI.fi will coordinate collection of data from existing initiatives, projects and reviews. Also interviews with key stakeholders will be performed. Additionally, BBMRI.fi will perform a telephone interview to Pharma contacts. The task has been initiated by listing of contacts from the participating National Nodes.

Task 2: Compliance with upcoming EU in vitro diagnostics regulation (M6-18; lead: BBMRI.fi; participants (lead: BBMRI.fi):

The plan is to produce a guideline for biobanks to comply with the upcoming EU in vitro diagnostics regulation. We aim to analyse and discuss the implications with external experts including EMA. The EU in vitro diagnostics regulation has now finalized by the EU and the latest version has been circulated to National Nodes. Currently, the search for contacts of National Nodes is ongoing.

The plan for next months:

- Determine major problems – specifically regarding sample properties
- Organise discussions with external experts

Task 3: Compliance with the European Committee for Standardization (CEN) and ISO standards (BBMRI.at):

In 2015 the European Committee for Standardization (CEN) has published eight CEN/TC140 Technical Specifications “In vitro Diagnostic Medical Devices” (CEN/TS):

- CEN/TS 16826-1, Snap frozen tissue – Part 1: Isolated RNA
- CEN/TS 16826-2, Snap frozen tissue – Part 2: Isolated proteins
- CEN/TS 16827-1, FFPE tissue – Part 1: Isolated RNA
- CEN/TS 16827-2, FFPE tissue – Part 2: Isolated proteins
- CEN/TS 16827-3, FFPE tissue – Part 3: Isolated DNA
- CEN/TS 16835-1, Venous whole blood – Part 1: Isolated cellular RNA
- CEN/TS 16835-2, Venous whole blood – Part 2: Isolated genomic DNA
- CEN/TS 16835-3, Venous whole blood – Part 3: Isolated circ. cell-free DNA from plasma

In 2016 one more Technical Specification was published:

- CEN/TS 16945 Metabolomics in urine, serum and plasma

[9] http://www.corbel-project.eu/home.html

Currently they are implemented in the new ISO standards ISO212 and ISO276. The aim of these CEN/TS and standards is to reduce the number of sample-based diagnostic mistakes, the number of non-reproducible pre-clinical as well as clinical studies and thus support the development of biomarkers.

In a first step BBMRI.at developed an MS Excel based checklist for the assessment of the compliance with the CEN/TS (snap frozen tissue - RNA and FFPE tissue - RNA). This list is based on the requirements and recommendations as stated in these CEN/TS (Fig 1). It allows users to evaluate if their pre-analytical processes are conform with the CEN/TS and the upcoming ISO Standards.

The checklist also serves as a supportive instrument for the user to cross-check his current SOPs and to adapt them according to the requirements of the CEN/TS and the upcoming ISO standards.

The Excel based checklist served as the basis and the requirement specification for a prototype of an online 'Self-Assessment Tool for Conformity with CEN/TS and ISO standards, which BBMRI.at developed in a second step. Several different IT-tools were analyzed with respect to their suitability as technical framework. The technical framework chosen for the online 'Self-Assessment Tool' is Research Electronic Data Capture (REDCap), an internationally well-established, mature and secure web application for building and managing online surveys and databases developed by the Vanderbilt University. It is easy to implement and allows an individual design of the data collection instrument and facilitates data exports, reports and basic statistics and logging.

This prototype has been introduced to the BBMRI-ERIC community and is currently optimized and extended to include all 9 CEN/TS for molecular in-vitro diagnostics examinations. The final Online Self-Assessment Tool, shall be ready by M18 (March 2017, D6.3-IT-tool for monitoring compliance of biobanks with CEN/TS for molecular diagnostics examinations).
(75% completed, 6 months remaining to completion)

Task 4: Optimal usage of -omics technologies (BBMRI.fi):
By contacting National Nodes, we will execute omics survey in selected biobanks and technology platforms to establish quality criteria and standard operating procedures for omics specific sampling, NGS, RNA transcriptomic, proteomic and metabolomics analyses. Additionally, we will produce a map of omics data for BBMRI-ERIC directory.

The omics survey will be initiated in National Nodes and the survey is combined with WP2 survey of technology platforms. The questionnaire has been designed and a core working group of National Node directors has been identified.

Task 5: Design of a biomarker Expert Centre for improved access for industry (BBMRI.at):
The aims of the Expert Centres are to provide efficient access for the industry to human biological samples for biomarker R&D, to engage industry in a public-private-partnership and to generate a single access point to BBMRI-ERIC resources and services. Building up awareness for distributed architecture of the biomarker Expert Centre should be generated, therefore, there is a must to invite all National Nodes to participate. This should lead into a well-organized implementation and trigger more interest from academia and industry.

BBMRI-ERIC published a guideline "BBMRI-ERIC-Associated Expert Centres / Trusted Partners V2.0". The guideline describes the BBMRI-ERIC Expert Centre model, the application criteria, the assessment and vote

process.

BBMRI.at supported the application of CBmed GmbH for becoming a BBMRI-ERIC-Associated Expert Centre/Trusted Partner. CBmed GmbH is an Austrian competence centre for biomarker research in medicine located at the Medical University Graz. CBmed GmbH links excellent research infrastructure, scientific expertise, medical knowledge, national and international industry partners. It has special emphasis on identifying new biomarkers, validating potential biomarkers and conducting translational biomarker research for products to be used in the clinical practice. In addition, CBmed GmbH has a strong link to the BBMRI.at-associated Biobank Graz, one of the largest biobanks in Europe.

Task 6 – Collaboration with other ESFRI-BMS research infrastructures, IMI, FP7 projects as well as national biomarker programmes (lead: BBMRI-ERIC):

Several meetings have taken place and participated by BBMRI-ERIC to foster the collaboration with IMI and FP7 projects. In February 2016 DELOITTE organised an online meeting in regards to IMI project sustainability plans for ABIRISK project. This was followed by an IMI initiated Workshop on biobank sustainability, BBMRI-ERIC also participated in ABIRISK General Assembly in April 2016. In September, BBMRI-ERIC participated the final Annual Meeting of BBMRI-LPC project where a session in LPC sustainability was held to finalise how the concepts and solutions of BBMRI-LPC can be continued within BBMRI-ERIC (incorporated into the BBMRI-ERIC Work Programme 2017). Further, during 2016 three different face-to-face meetings were organised with EMA to increase the collaboration and seek future interaction opportunities (e.g. Good biomarker practice, and an Academia framework of collaboration).

In terms of RI collaboration, eight BMS Research Infrastructures (BBMRI, EATRIS, ECRIN, ELIXIR, EU-OPENSCREEN, INFRAFRONTIER, ISBE and MIRRI) have worked together to formulate views on how RIs can contribute to challenging areas of personalized medicine in Europe. This work was initiated on discussions during CORBEL project retreat in April 2016. As a result, a joint paper has been written on how different RIs are able to contribute to the challenges of personalised medicine today (to be submitted in European Journal of Human Genetics). Further, BBMRI-ERIC is now representing European research infrastructures in the International Consortium for Personalised Medicine (IC Permed).

WP7 – Common Service for Rare Diseases

Work Package leader: Luca Sangiorgi, BBMRI.it
Co-leader: Gert-Jan van Ommen, BBMRI.nl

Task 1 – Coordination of efforts and achievements of different projects involving RD biobanks, registries and infrastructures and to provide a sustainable base for biobanking activities within the RD community (lead: BBMRI.nl):

Many RD research projects have developed biobanks and registries as part of their efforts to allow access to samples and data for research and clinical trials. Moreover, several overarching projects have contributed to this area and developed shared tools and unified platforms. The coordination and integration of existing biobanks and resources and the development of further expertise are the focus of this task. In order to provide

a sustainable base for biobanking activities within the RD community:

Kick off Meeting ADOPT BBMRI-ERIC (October 2015)
RD-CONNECT ANNUAL MEETING (March 2016)
EUROBIOBANK Assembly meeting (March 2016)
ADOPT BBMRI ERIC MEETING (March 2016)
ADOPT BBMRI ERIC AoM#6 (April 2016)
ECRD 2016 : The European Conference on Rare Diseases & Orphan Products (May 2015)
RD-ACTION Workshop: 'Exchanging data for virtual care within the ERN Framework (September 2016)
Europe Biobank Week, Patient and ELSI sessions. (September 2016)

Task 2 – Define specific quality standards for samples and data in the context of rare diseases to match quality criteria and procedures of existing rare diseases biobanks with the requirements of BBMRI-ERIC (lead: BBMRI-ERIC):

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
- 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 pre-examination 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).

- CEN/TS 16826-1, Snap frozen tissue – Part 1: Isolated RNA
- CEN/TS 16826-2, Snap frozen tissue – Part 2: Isolated proteins
- CEN/TS 16827-1, FFPE tissue – Part 1: Isolated RNA
- CEN/TS 16827-2, FFPE tissue – Part 2: Isolated proteins
- CEN/TS 16827-3, FFPE tissue – Part 3: Isolated DNA
- CEN/TS 16835-1, Venous whole blood – Part 1: Isolated cellular RNA
- CEN/TS 16835-2, Venous whole blood – Part 2: Isolated genomic DNA
- CEN/TS 16835-3, Venous whole blood – Part 3: Isolated circ. cell-free DNA from plasma

- CEN/TS 16945 Metabolomics in urine, serum and plasma
- Others to be examine more closely

Task 3 – Map procedures and tools already available in BBMRI-ERIC and adapt for RD biobanking (BBMRI.nl):
The objectives are to promote actions to integrate RD-CONNECT biological sample catalogue with JRC registries, thus developing the BBMRI-ERIC portal as an online RD biobank catalogue and ID-cards for RD biobanks according to BBMRI standards. ID cards of RD-CONNECT already work since more than a year, available at: http://catalogue.rd-connect.eu/.

Task 4 – Establish a Help-desk facility to provide real-time support to RD biobanks and/or registries to meet requirements for participation to BBMRI-ERIC (lead: IOR):
Common Service IT as a part of collaboration between WP3 (IT) and WP7 of ADOPT has installed a Helpdesk application -- Request Tracking system. This system allows users from both inside and outside of BBMRI-ERIC to submit their requests and assign these requests to the responsible people and monitor progress of their completion. A dedicated queue for RD has been setup within the HelpDesk, together with introductory training of several selected people. For the next period of the project, it is expected that WP3 will support operations of the Helpdesk and deliver minor modifications based on the requests of WP7.

Further main activity on WP7 has focused on the study of literature on models for Helpdesk and the document describing the Helpdesk facility. WP7 has had staff meetings and conference calls with the ADOPT partners and representatives of the Common Service IT.

Registry/biobank Help-desk facility develops selecting as a model Tiered Structure - Generalist Model and it provides a layered structure with requests to three possible levels, and three possible levels of assistance. Support will be delivered according with RD-CONNECT biobank assessment criteria, to ensure adherence to minimal entry conditions and the adoption of any standardisation and harmonisation measures needed for a successful biobank. Interested biobanks must already store collections of rare disease biological samples

Biobanks should have a quality system in place for the operational management, including quality assessment/quality control for sample and data management. QS for sample management should follow best practice guidelines such as those of the OECD, BBMRI-ERIC Quality Policy and applicable European standards for pre-examination processes for human specimens.

In collaboration with BBMRI.at (MUG, D6.3 – IT-tool for monitoring compliance of biobanks with CEN/TS for molecular examinations) who has generated an Excel list and a prototype of an online Self Assessment Tool based on the CEN/Technical Specifications, BBMRI-ERIC further develops the Self Assessment Tool. Based on this prototype and on the defined applicable Guidelines, Best Practices and International Standards (D7.3) the Self Assessment Surveys will be published and available for the BBMRI-ERIC members (as listed above under the CEN/Technical Specifications for pre-examination processes).

The biobank should have adopted SOPs regulating: sample (and data) acquisition, testing to ensure sample (and data) integrity and sample processing and storage. The biobank should also adhere to the following ELSI principles: 1) samples are collected only if an appropriate informed consent has been previously obtained by the donor 2) the consent can be withdrawn and sample (and data) removed anytime by the donor 3) contact person is available for donor enquiries regarding ethical and legal issues, such as informed consent, its withdrawal, or the use of the samples 4) confidentiality issues need to be dealt with in compliance with the local government laws 5) specific rules and policies for distributing samples (and data) are clearly defined.

The biobank should meet the following minimum IT-system requirements: 1) centralised or distributed data repository 2) information Management system to manage biobank repositories, resources, samples and data in a structured way 3) data identification capabilities (local persistent unique identifiers for samples and sample data) 3) data transfer capabilities (exportability of data from the management system to a file format and secure data transfer through the internet).

The Helpdesk offers three possible levels:
Level 1: Wiki system, Frequently Asked Questions (FAQs) and Guideline Repository
Level 2: Ticketing, Data collected from questions/answers in a repository – user experience and video FAQs (from different biobanks)
Level 3:On particular aspects such as the Ethics Legal and Social Issues (ELSI), the help desk aims to manage directly the site or service interest:

- BBMRI-ERIC Directory to individuate biobanks typology and main information
- BBMRI-ERIC Common Service ELSI, to manage potential questions on ELSI
- BBMRI-ERIC-HQ Quality Service provides consultancy related to Quality Management http://www.bbmri-eric.eu/wp-content/uploads/2016/08/BBMRI-ERIC_QM_Services_final.pdf
- For all questions on Rare Disease, a bridge of knowledge and competences between RD-Connect and the beginning RD ERNs.

At the beginning, the first implemented level will consist of a web service level 1., hereinafter; the level 2 and eventually the level 3 of the Helpdesk facility will be implemented. The Helpdesk will finally be tested as a transversal service on ERN on Rare Bone Diseases: as a common service between BBMRI-ERIC and RD-CONNECT. The Helpdesk facility implemented within BBMRI-ERIC and ADOPT project will be further tested by Working Groups: “Multidisciplinary Care-eHealth Tools”, and “Research” in BOND ERN.

Task 6 – Develop a governance model for the sustainability of RD biobanks that allows well operating RD biobanks to continue their operation within BBMRI-ERIC (lead: BBMRI-ERIC):
BBMRI-ERIC together with BBMRI.nl started to work on sustainability of the RD cataloguing using BBMRI-ERIC Directory as a platform. As a first step to achieve the milestone "Milestone: RD-Card for RD Biobanks (M12)", the Directory 2.5 has implemented an extended data model that supports mapping of identifiers and interlinking between RD-CONNECT Catalogue and BBMRI-ERIC Directory.

Task 7 – Pilot Study on Osteogenesis imperfect (lead: IOR):
The User Case will be conducted in collaboration with RD-CONNECT. For this, the following meetings were organized: Round Table Niklas Blomberg (ELIXIR), Meeting with Hanns Lochmüller and Rachel Thompson -RD-CONNECT , and RD-CONNECT and EuroBIOBANK meeting invitation.

User Case on Osteogenesis Imperfecta:
Merging of registries of 700 patients with 700 biobanked samples. Imaging data:

- X-Rays, Ultrasound, MRI
- Unstructured
    - Annotation
    - Location (distributed)
    - Updates/’versioning’
- NGS panel data (done)
- Exome data (work in progress, dep. on selection criteria)

The User Case on Ostegenesis Imperfecta will give the opportunity to conduct an ELIXIR-BBMRI-ADOPT combined study, with the following objectives:

- To make the key data items linkable,
- To recommend approach towards decision support,
- To apply the linkable data for specific tasks outcomes,
- To test interoperability components for achieving linkability

ELIXIR Implementation Study title: "FAIR ERNs: Testing FAIR data principles to support European Reference Networks by increased interoperability of clinical and biomedical data, test case: Osteogenesis Imperfecta".

WP8 – Internationalisation
Work Package leader: Markus Pasterk, BBMRI-ERIC

Task 1 – Country mapping (lead: BBMRI-ERIC):
Country mapping was completed in order to identify which countries in principle would benefit from a membership at BBMRI-ERIC and should therefore be contacted for admission. The work was done by screening all published National Research Infrastructure roadmaps, the ERA roadmaps and other official documents mentioning BBMRI or biobanking. This review revealed that the table of National RI roadmaps published the EC website is somewhat outdated as many more new roadmaps or updates could be found by using simple 'google approach'. All "old" EU member states showing biobanking activities in their National RI roadmaps are already members of BBMRI-ERIC or in the status of applying soon (Ireland). The "missing" countries Spain, Denmark and Portugal do not prioritize Biobanking within their National roadmaps and for Luxembourg and Iceland no roadmaps are published. From the "new" EU members, Bulgaria, Hungary, Slovenia, Lithuania are not yet members but refer to BBMRI in their roadmaps. Poland, Estonia, Latvia, the Czech Republic and Cyprus are already integrated into BBMRI-ERIC. Report on the country mapping activity was given during the BBMRI-LPC Forum in September 2017.

Task 3 – Africa and Low Middle Income Countries (lead: BBMRI-ERIC):
The existing links between Europe and Africa were strengthened by liaising with scientist involved in Africa related activities such as BCNet initiative with IARC to jointly address the many challenges of biobanking.

Task 4 – China (lead: BBMRI-ERIC):
BBMRI-ERIC has been involved in liaising with Chinese experts from Shanghai, Beijing and Shengzen. It was agreed to host a train-the-trainer workshop in Europe on how to implement the new CEN norms for quality management. This workshop was hosted at the University of Nice during May 2016. The Chinese trainer shall be the core staff for a bigger workshop of the same content in China at a later time point.

Task 5 – United States/Canada (lead: BBMRI-ERIC):
Activities in United States/Canada include contacts with United Nations, which let to an invitation to present BBMRI-ERIC at a European Alliance for Personalised Medicine High-level Workshop in September 2016. The first concrete result of the MoU signed with P^3G was the joint efforts to organise the 2016 Europe Biobank Week together with ESBB and BBMRI-LPC.

5. Resources Review (M1-M12)

n/a ***Linked 3rd party to BBMRI-ERIC**

M1-12	WP1		WP2		WP3		WP4		WP5		WP6		WP7		WP8		Total		Unused	**Spent**
	Planned	Actual	Planned	Actual	Planned	Actual	Planned	Actual	Planned	Actual	Planned	Actual	Planned	Actual	Planned	Actual	Planned	Actual	PMs	**%**
BBMRI-ERIC	5,0	15,6	1,0	0,6	190,0	1,7			63,0	1,6			7,6	1,0	0,1	0,1	266,7	20,5	246,2	**7,7**
***UNIMIB**	0,5	0,2	9,0	3,0	1,0	0,3	2,0	0,3			1,0	0,0	1,9	0,0			15,4	3,8	11,6	**24,4**
***UM**	0,5		1,0		4,0		1,0				1,0		1,9				9,4		9,4	
***MUG**	0,5	0,0	1,0	0,0	26,0	4,4	1,0	0,0			7,0	5,4	1,9	0,0			37,4	9,8	27,6	**26,2**
***THL**	0,5	0,2	1,0	0,1	12,0	0,0	1,0	0,0			7,0	0,0	1,9	0,0			23,4	0,4	23,1	**1,5**
BCR	0,5	0,2	1,0	0,1	4,0	1,5	1,0	0,0			1,0	0,0	1,9	0,0			9,4	1,9	7,5	**19,8**
SNF	0,5		1,0		1,0		1,0				1,0		1,9				6,4		6,4	
MOU	0,5	0,1	1,0	0,2	1,0		1,0	0,1			1,0	0,2	1,9				6,4	0,6	5,8	**9,7**
CHARITE	0,5	0,0	1,0	0,0	3,0	0,0	1,0	0,0			1,0	0,0	1,9	0,0			8,4	0,0	8,4	**0,0**
UTARTU	0,5	0,4	1,0	0,4	4,0		1,0				1,0	0,2	1,9				9,4	1,0	8,4	**10,6**
INSERM	0,5		6,0		1,0		2,0				1,0		1,9				12,4		12,4	
BRFAA	0,5		1,0		2,0		1,0				3,0		1,9				9,4		9,4	
LUMC	0,5		1,0		1,0		1,0				1,0		2,4				6,9		6,9	
UMCG					8,0												8,0		8,0	**0,0**
NTNU	0,5		1,0		1,0		1,0				1,0		1,9				6,4		6,4	
WRC EIT+	0,5	0,0	1,0	1,4	1,0	0,1	1,0	0,0			1,0	0,0	1,9	0,0			6,4	1,4	5,0	**22,2**
KI	0,5	0,0	1,0	0,8	1,0	0,8	1,0	0,8			1,0	0,7	1,9	1,4			6,4	4,4	2,0	**68,4**
DOKUZ	0,5		1,0		1,0		1,0				1,0		1,9				6,4		6,4	
IARC	0,5		1,0		1,0		1,0				1,0		1,9				6,4	1,5	4,9	**23,4**
TUM					2,0	0,9	0,0										2,0	0,9	1,1	**45,0**
IOR	0,2	0,2															0,2	0,2	0,0	**100,0**
UCL	0,5	0,0	0,5	0,0	1,0	0,0	0,3	0,0					1,5	0,0			3,8	0,0	3,8	**0,0**
DKFZ					37,0	8,8											37,0	8,8	28,3	**23,6**
FAU					37,0	4,5											37,0	4,5	32,5	**12,2**
Total	**14,2**	**16,9**	**31,5**	**6,6**	**340,0**	**22,9**	**19,3**	**1,2**	**63,0**	**1,6**	**31,0**	**6,5**	**41,9**	**2,4**	**0,1**	**0,1**	**541,0**	**59,6**	**481,4**	**11,0**
Unused PMs		-2,6		25,0		317,1		18,1		61,4		24,5		39,5		0,0				
Spent %		118,4		20,8		6,7		6,0		0,0		21,1		5,8		100,0				