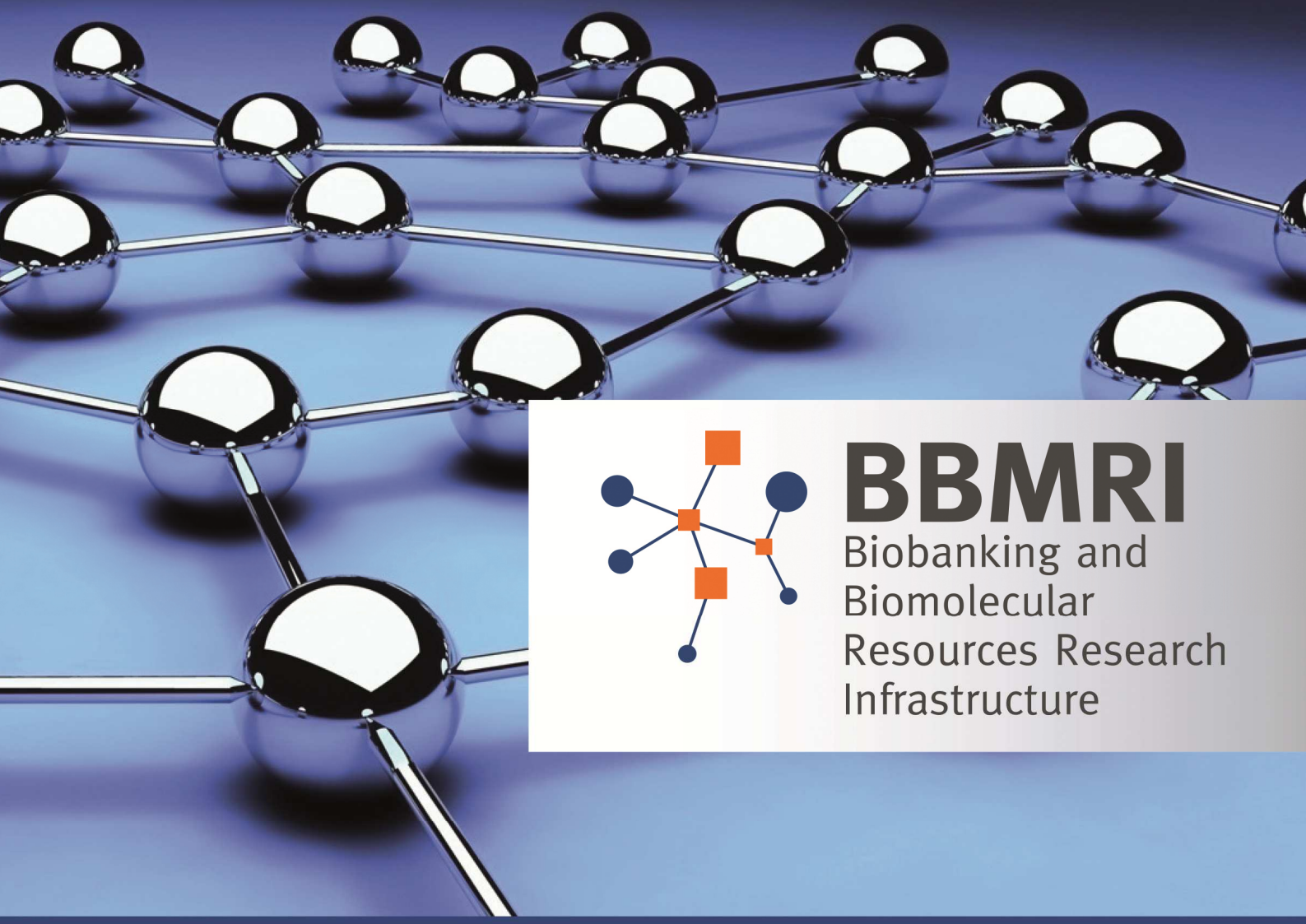

BBMRI
Biobanking and Biomolecular Resources Research Infrastructure

Business Plan

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Scientific representative of the project's coordinator:
Univ. Prof. Dr. Kurt Zatloukal, Medical University of Graz,
Auenbruggerplatz 25, A8036 Graz, Austria
Tel: +43 316 380 4404
Fax: +43 316 384 329
E-mail: Kurt.zatloukal@medunigraz.at

Website: www.bbmri.eu

Preface

This business plan is based on the planning work performed by the consortium that participated in the preparatory phase of the European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI). The first part of the business plan is structured according to the requirements of the ERIC Council regulation (EC) No 723/2009 whereas chapters 3 - 11 provide the information as requested under Article 4 (Requirements relating to infrastructure). The second part (chapter 12) describes in addition the budget required to implement and operate BBMRI under the ERIC legal framework.

Further details are provided in the Annexes. The Annexes include information on Common Information Technology Service that provides the technical solutions for efficient data sharing and protection of privacy. The common service for Ethical, Legal and Societal Issues that supports and supervises ethical and legal compliance. The Partner Charter desribes minimal criteria for biobanks and biological resource centres of BBMRI-ERIC Members to become affiliated with the infrastructure. Details of the cost items of the Central Executive Management Office and the Common Services are provided in Annex VI. Furthermore the Annexes contain the consensus text of the Memorandum of Understanding of EU Member States to support the implementation of BBMRI under the ERIC legal framework.

The business plan provides reference to the Statutes of BBMRI-ERIC in several chapters. These references are not complete quotations of the Statutes and, therefore, only the Statutes represent the legally relevant wording.

For the BBMRI Preparatory Phase consortium:

Kurt Zatloukal	Eero Vuorio	Georges Dagher
(Coordinator)	(Executive Manager)	(WP leader Funding and Finances)

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2. Executive Summary

Biological resources, such as cells, tissues or biomolecules are considered as the essential raw material for the advancement of biotechnology, human health, and for research and development in life sciences. The pan-European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) improves the accessibility and interoperability of the existing comprehensive collections, either population-based or clinical-oriented, of biological samples from different (sub)populations of Europe. These collections include the attached data on factors such as health status, nutrition, lifestyle, and environmental exposure of the study subjects. Combined with the expertise of the clinicians, pathologists, bio-informaticians, and molecular biologists involved, a globally unmatched, Europe-wide platform for translational medical research is envisaged with the aim to develop personalised medicine and disease prevention for the benefit of European citizens. In particular, BBMRI will ensure sustainable access to key resources required for science-based responses to several of the health-related grand challenges, such as sustainable health care for ageing population, new pandemics, and security threats. To reach this goal, also biotech and pharmaceutical industry must have a possibility to collaborate with academic researchers in order to fully realise the enormous potential of European biobanking. In addition to clinical, ethical and legal experts, patient communities are involved to achieve standards and guidelines that properly balance individual values, such as protection of privacy and informed consent, with shared values of facilitated access to progress in health care and disease prevention.

This can only be achieved by a distributed research infrastructure with operational units in most, if not all, European Member States. BBMRI is going to be implemented under the ERIC (European Research Infrastructure Consortium) legal entity. BBMRI-ERIC foresees a Central Executive Management Office ("Headquarter") in Austria that coordinates the interaction of National Nodes established in several Member States. The Central Executive Management Office provides a common access portal to resources available at BBMRI-ERIC Partners as well as appropriate facilities and expertise. The National Nodes are also established under the ERIC legal entity and link the national scientific community (e.g., biobanks, universities, hospitals, research institutions, and resource centres) to BBMRI-ERIC. The participation in BBMRI-ERIC and the governance of BBMRI-ERIC are defined in the statutes of BBMRI-ERIC. The interaction between BBMRI-ERIC and the Partners is defined in the Partner Charter that has to be agreed between National Nodes and Partners. This distributed architecture of BBMRI-ERIC also enables distribution of some management tasks (e.g., Common Services) to BBMRI-ERIC Members, and promotes positive impact on regional development in all participating Member States.

The Mission

BBMRI-ERIC will increase efficacy and excellence of European bio-medical research:

- by facilitating access to quality-defined human health/disease-relevant biological resources including associated data in an efficient and ethically and legally compliant manner,
- by reducing the fragmentation of the bio-medical research landscape through harmonization of procedures, implementation of common standards and fostering high-level collaboration,
- by capacity building in countries with less developed biobanking communities thereby contributing to Europe's cohesion policy and strengthening the ERA.

BBMRI-ERIC will provide access to the collections of BBMRI-ERIC Partner Biobanks and Biomolecular Resources, their expertise and services on a non-economic basis by providing:

access to samples and related clinical data based on the scientific excellence of the proposed project as determined by an independent peer review and on ethical review of the research project proposal.

free access to documents, Standard Operating Procedures (SOP's) and best practices developed by BBMRI-ERIC,

BBMRI-ERIC shall seek to ensure that the source of samples and data be appropriately acknowledged and should request that such attribution be maintained in subsequent use of the samples and data.

BBMRI-ERIC also foresees special solutions to facilitate access for industry through Expert Centres that can be established as public-private-partnerships and are associated with BBMRI-ERIC. Expert Centres perform the primary analysis of biological samples in a pre-competitive setting using latest technologies under standardized conditions, and operate on a non-for-profit basis. Data generation in Expert Centres will also lead to more efficient use of finite resources and improves sharing of the research data generated. Expert Centres will also lead to a repositioning of intellectual property and enhance competitiveness of Europe's large industry as well as SME's by fostering collaboration thereby contributing to the goals of the Innovation Union Initiative.

Incentives for countries to become BBMRI-ERIC members comprise:

- Increased competitiveness of national scientific community because participation of a country in BBMRI-ERIC will exert - and has already exerted - a major positive impact on the structuring of national scientific community, and BBMRI-ERIC will provide a framework for high level international collaborations.
- Increased efficacy of investments into the national scientific community by avoidance of double investments into common requirements by sharing solutions on IT and data management, biobanking technologies, standardization and quality management, ethical and legal issues.
- Playing an active role within the European biobanking landscape by active participation within BBMRI governance structures (e.g. Management Committee, Common Services).
- Participation in specific training programmes those are restricted to BBMRI-ERIC members.
- Impact on Innovation and regional development.
- Global recognition and impact of national developments because BBMRI-ERIC will become a leading global organization for biobanking and biomolecular resources.
- Reduced fees for access and project processing.

A specific goal of BBMRI–ERIC is the promotion of increased participation of Eastern and Southern European countries in order to establish a pan-European research area in this field. This should be achieved by education and training programmes, supporting the development of biobanks and biobanking technologies, and developing joint research and innovation regions. For this goal funding by Structural Funds and using funding instruments of the European Investment Bank is planned.

The operation of BBMRI-ERIC should be financed by a common BBMRI-ERIC budget for the Central Executive Management Office and the Common Services. National Nodes will be financed through national budgets. A start-up phase is planned from 2013 - 2015, and full implementation should be achieved by 2016. It is expected that at least 10 Members will participate in the foundation of BBMRI-ERIC since 10 countries have already committed in total of 135 Mio€ to establish the national BBMRI nodes and 14 Member States (Austria, Bulgaria, Czech Republic, Estonia, Finland, France, Greece, Italy, Latvia, the Netherlands, Malta, Spain, Sweden, Norway) have signed the Memorandum of Understanding to implement BBMRI-ERIC.
The cost of establishing BBMRI-ERIC European coordination is estimated to be about 2 Mio€/year during the start-up phase and about 3 Mio€/year after full implementation in 2017, financed through Member contributions, EU-funding, and access fees. The annual contribution of individual Members may actually decrease as the number of BBMRI-ERIC Members grows in case of successful funding of some activities by EU-grants.
In case BBMRI-ERIC will be established with 8 or less founding Members or the European economic situation is worsening a minimal budget for basic operation of BBMRI-ERIC is foreseen. The minimal budget is based on 1.113 k€ total annual contribution of Member States. The Member State contribution can be frozen at this level for several years until more Members join BBMRI-ERIC or the economic situation improves.

BBMRI-ERIC minimal annual budget

EXPENDITURES	**k €**
Central EM Office	810
IT node	239
ELSI Platform	119
Stakeholder Forum	81
Common Biobanking and Resources Services	0
Total Expenditures	**1.249**
INCOME	
Member States	1.113
Research Grants	0
Hosting Countries	124
Access Fees	12
Total Income	**1.249**

3. Terminology

Assembly of Members

The Assembly of Members is the decision making body in BBMRI-ERIC. It is composed of representatives from BBMRI-Members (e.g., Member States, associated countries, third countries, intergovernmental organizations).

Biobanks and Biological Resources Centres (according to the OECD definition, 1998)

“Biobanks or Biological Resources Centres (BRCs) are an essential part of the infrastructure underpinning life sciences and biotechnology. They consist of service providers and repositories of the living cells, genomes of organism, and information relating to heredity and the functions of biological systems. Biobanks or BRCs contain collections of culturable organisms (e.g. micro-organisms, plant, animal and human cells), replicable parts of these (e.g. genomes, plasmids, viruses, cDNAs), viable but not yet culturable organisms, cells and tissues, as well as databases containing molecular, physiological and structural information.

BBMRI-ERIC will focus on all types human biological samples and related data as well as biomolecular resources including model- and micro-organisms that might contribute to the understanding of the physiology and diseases of humans.

Central Executive Management Office

Is located in the BBMRI-ERIC hosting country and manages the operation of the European infrastructure. The Central Executive Management Office is lead by the Director General.

Common Services

BBMRI-ERIC aims to provide to its users expertise, services and tools to implement the Work Programme of the infrastructure by establishing and supporting Common Services (such as sample and data access, ethical and legal services, information technology services). Common Services are established under BBMRI-ERIC and are placed under the responsibility of the Director General. Each of these Common Services is managed by a Director, appointed by the Director General after consultation with the national delegates of the hosting Member State and acting on his/her behalf. Directors of Common Services participate in the operational management of BBMRI-ERIC as members of BBMRI-ERIC Management Committee.

Hub-and-Spoke Structure

Hub-and-Spoke-Structure refers to the federated IT-architecture developed to link national biobanks to National Nodes that are integrated into BBMRI-ERIC which provides one common access point for users.

National Node

A National Node means an entity, not necessarily of legal capacity, designated by a Member State, that coordinates the national *Biobanks and Biolmolecular Resources*, and links its activities with the pan-European activities of BBMRI-ERIC. Each National Node has a Director, appointed by an appropriate authority of the Member State, hereinafter referred to as “National Coordinator”. The National Coordinators participate in the operational management of BBMRI-ERIC through participation in the BBMRI-ERIC Management Committee.

Management Committee

The Management Committee shall be established by the Director General and comprises the Coordinators of *National/Organizational Nodes* and *Common Services*. The Management Committee will play a key role in developing the Work Programme and in supporting its execution by coordinating the interactions of the key elements of BBMRI-ERIC and the national scientific communities.

Scientific and Ethical Advisory Board (SEAB)

The Scientific and Ethical Advisory Board comprises of distinguished scientists or experts appointed in their own right who advise the Assembly of Members as well as the Director General on the realization of the Work Programme.

Scientific Review Board and Ethical Review Board

For the operation of BBMRI-ERIC, the Director General and the BBMRI-ERIC Management Committee will also establish a Scientific Review Board (SRB) and an Ethical Review Board (ERB) consisting of international high level experts for scientific and ethical review of research proposals received by the Central Executive Management Office.

Stakeholder Forum

The Stakeholder Forum comprises representatives from industry, medical associations, scientific associations and patient organizations. The Stakeholder Forum will be supported by a Secretariat that is established under BBMRI-ERIC. The Assembly of Members shall decide how it will organize the Stakeholder Forum.

Work Programme

"***Work Programme***" means the description of the strategy, planned activities, staffing and funding of BBMRI-ERIC. It is developed by the Director General with the contribution of the BBMRI-ERIC Management Committee and is adopted by the Assembly of Members.

4. User needs and scientific challenges

4.1 Biobanks in medical research and development

Human biological samples, such as blood, tissues, cells or DNA, plus associated clinical and research data, as well as biomolecular research tools are key resources in unravelling genetic and environmental factors underlying diseases and influencing their outcome (Collins et al., 2003; Manolio et al., 2006). Furthermore these resources are required for identification of new targets for therapy and may help to reduce attrition in drug discovery and development. Consequently, biological resources are considered as the essential raw material for the advancement of biotechnology, human health and research and development in life sciences (OECD, 2001). According to the ESFRI roadmap, the pan-European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI-ERIC) is designed to further develop these resources and to provide access to academia and industry (ESFRI, 2008).

Following the rapid progress in genomics research of humans and their ancestors, biomedical and health research has expanded from the study of rare monogenic diseases to common, multifactorial diseases. Innovative, high-throughput technologies are widely expected to enable a better dissection of these complex, causally heterogeneous diseases into more specific diagnostic entities, which is a requirement for the advancement of personalised medicine (Collins et al., 2003). A sharper, biology-based definition of disease categories will enhance the development of more effective treatment, reduce undesired side effects of new treatments, improve success in clinical trial design, and will lead to new concepts of disease prevention. Elucidation of complex disease aetiology is challenging because diseases are caused by a large number of small, often additive effects, representing the sum of the consequences of genetic predisposition, lifestyle and the environment.

Revealing these complex interactions will depend critically on the study of large sets of well-documented, up-to-date epidemiological, clinical, biological and molecular information and corresponding material from large numbers of patients and healthy persons, collected and made available by biobanks (Hagen and Carlstedt-Duke, 2004). The biological material collected in biobanks for biomedical research typically comprises DNA, tissues, cells, blood, other body fluids as well as pathogen-containing biological samples. Although currently established biobanks and biomolecular resources are a specific European strength, valuable and irreplaceable national collections typically suffer from fragmentation of the European biobanking-related research community, variable access rules, the lack of commonly applied standards, lack of interoperability of clinical, analytical and -omics datasets required for research, and a diversity of legal procedures and ethical considerations (European Science Foundation, 2008). This hampers the collation of biological samples and data from different biobanks which is a prerequisite to achieving sufficient statistical power and to avoid selection bias. Moreover, it results in duplication of effort and jeopardises sustainability because of the lack of long-term comprehensive funding approaches.

There is also a need to strengthen the capacity to develop networks of biobanks meeting high standards of integration compatible with the design of studies structured as Phase II or III clinical trials. This type of study design is essential for validation and translation of biomarkers into clinical practice.

Ultimately, BBMRI-ERIC will favour the study of important biomedical research questions that are beyond the scope of efforts of single Member States. Short-term benefits will appear soon, such as increased quality and speed as well as reduced cost of research through better coordination. It will provide a service platform to achieve long-term sustainability of outcomes of EU-funded projects and programmes that establish collections of biological materials, develop databases or generate biomolecular research resources. Because of the pan-European scale BBMRI-ERIC will become an effective measure to reduce fragmentation of the European research landscape and increases competitiveness through collaboration. In close interaction with other research infrastructures from the biological and medical sciences BBMRI-ERIC will exert a major role in shaping the European research landscape there by positioning Europe's research in the global context. Longer perspectives include increased efficacy of drug discovery and development, and finally novel possibilities in health care (such as personalised medicine and science-based solutions for healthy ageing) and secured European competitiveness in research and health-related economy. The scientific as well as socioeconomic impact of biobanks and their integration in to transnational networks has been retrospectively assessed in a study performed by the Bureau d'economique theorique et appliquee (BETA; Strasbourg), and parameters that can be used to evaluate

the impact of BBMRI-ERIC in prospective manner have been elaborated by Technopolis (Technolopolis Group, The Netherlands) (Annex VII).

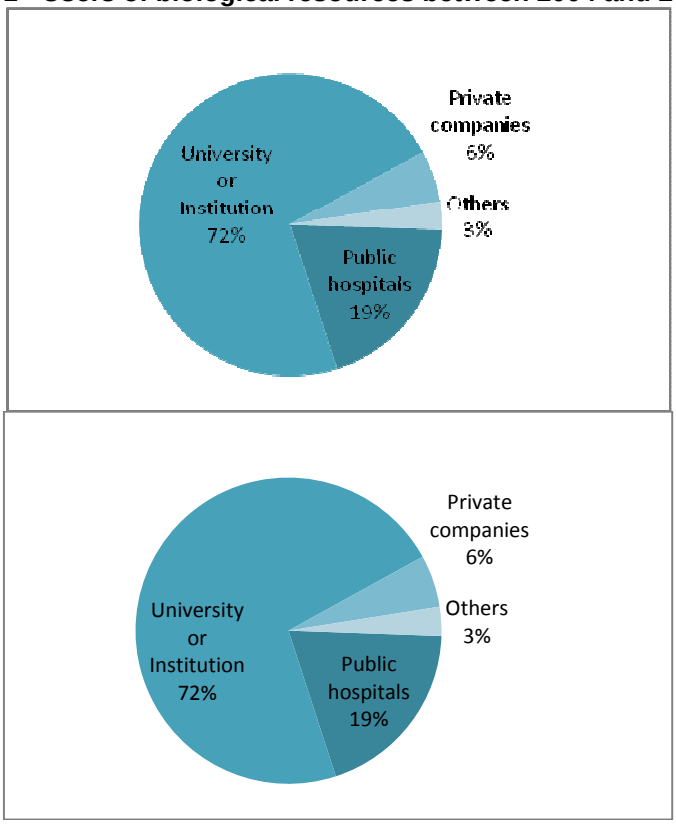
4.2 The BBMRI-ERIC user community

Due to the large diversity of biomedical fields using collections of biological material it is difficult to provide an accurate number of potential users of the future BBMRI-ERIC. A search by key words in *pubmed* bibliography is an inappropriate approach as terms such as biobanks, BRCs or biological resources are not included in regularly used indexes (Cambon-Thomsen, 2003). Nevertheless, during the preparatory phase BBMRI made some attempts to characterise and estimate the size of the future user community. According to a survey within 45 biobanks located within 8 BBRMI participating countries 91% of the users are from the public sector and include researchers from public hospitals, universities and research institutions. Private companies represent 6% of the users (Fig. 1). In addition, some BBMRI participating countries do provide partial data on the number of users. For instance, in France 600 public research groups using collections of biological material published about 2000 papers in the past five years. Another survey investigated the number of European research consortia that were funded by the health programme within the EU 7th framework program. The result revealed that about 120 European consortia have used or are currently using collections of biological material as resource for their investigations.

Based on these figures it is estimated that in the first year of the BBMRI-ERIC construction phase 12 to 15 European framework programme funded consortia would use its services, in addition to about 60 projects funded by other agencies. A 20% annual increase of this latter number is expected for the next 5 years.

Some of the recently established Joint Programming Initiatives (e.g. on neurodegenerative diseases) are also closely related to biobanked samples and data, and therefore would benefit from BBMRI-ERIC.

Fig. 1 - Users of biological resources between 2004 and 2009[1]



[1] Results from 45 out of 216 participating biobanks (20%) from 8 countries. BBMRI Supplementary Questionnaire – Outcome of Research using biological resources, 2009 - Others: Private foundations, Thematic Research Centre etc.

BBMRI-ERIC operates as a platform for exchange between European researchers from the public as well as from the private sectors, allowing the development of cutting edge projects and facilitating innovation processes. The aim is to foster high quality collaborations and the emergence of public-private partnerships.

4.2.1 Users from public sector: opportunities to develop large scale projects

Three types of users from public sector, each one interested in specific facilities provided by BBMRI-ERIC, have been identified: academic researchers, biobankers, international or national organizations (Table 1).

Table 1 - Types of users from public sector and their interest in BBMRI-ERIC

Academic researchers	Biobankers	International or national organizations
Interested in: accessing to collections of biological resources through the Web-based catalogue; assessing feasibility of the research projects; scientific counselling; advices on ethical and regulatory issues; planning of multinational prospective studies.	Interested in: biocomputing facilities, open source IT-solutions; SOPs, advices in quality management and certification as well in ethical, legal and societal issues; improvement of interoperability; shared efforts to reduce costs.	Interested in BMRI-ERIC expertise on subjects such as: biomedical research, biosecurity, (re)emerging pathogens; using biobanks to assess efficacy of healthcare, identify causes of inequalities in health care and large epidemiological studies.

4.2.2 Users from private sector: a high potential of development

Four types of users from private sector, each one interested in specific facilities provided by BBMRI-ERIC, have been identified: pharmaceutical industries, diagnostic industries and biotechnology industries (Table 2).

Table 2 - Four types of users from private sector and their interest in BBMRI-ERIC.

Pharmaceutical industry	Diagnostics industry	Biotechnology industry	Biospecimen processing industry
BBMRI-ERIC operations and services may help to identify new targets for therapy; reduce attrition in drug development; provide information on diversity of diseases as basis for clinical trial design; high interest in international harmonization of processes	Samples that meet requirements of latest –omics technologies; standardized pre-analytical processes; high interest in international harmonization of processes	Access to human biological samples, medical data, biomolecular resources, and expertise; biobanking services, access to expensive analytical platforms	Biobanking and biospecimen research itself is becoming an increasing market; BBMRI-ERIC will be a major customer and strategic partner for product development; key products: cryo-technology, plastic ware, research reagents and instrumentations for sample pre-analytics, RFID-technology, data bases, data security, biosafety, biosecurity

5. Planning of the Construction of BBMRI-ERIC

5.1 The BBMRI Preparatory Phase

BBMRI is one of the infrastructure projects that has been approved by the European Strategy Forum on Research Infrastructures (ESFRI) and set on the first ESFRI roadmap (ESFRI, 2006). In order to refine the concept of this future European infrastructure a three-year preparatory phase has been funded by the 7th EU framework program. In its preparatory phase BBMRI involved more than 270 Institutions from 33 countries, including biobanks, research institutions, several ministries and funding organizations (see Annex I). Seven work packages addressed the key issues relevant to further construction and operation of BBMRI. The work packages have been led by leaders in the fields and focussed on requirements of different biobank formats (e.g., population-based and clinical-oriented biobanks), biomolecular resources, data management and biocomputing, ethical, legal and societal issues, as well as funding and financing (Yuille et al., 2008). The solutions developed have been intensively discussed with external experts, users and stakeholders, and has been published, and presented to the public to ensure broad and sustainable acceptance (BBMRI's Stakeholder Forum, 2009, 2010; Bevilacqua et al., 2010) (Table 3).

Table 3 - Stakeholder and public engagement events

17 March 2007	Partner and Stakeholder Meeting, Vienna/Austria
10-12 February 2008	Kick-Off Meeting, Hinxton/UK
18 April 2008	BBMRI 1st Governance Council Meeting, Florence/Italy
28 May 2008	Seminar at the European Parliament, Brussels/Belgium
17-18 December 2008	Expert meeting on specific requirements for biobanking in Pathology, Laboratory Medicine, and rare diseases
25-27 March 2009	PHOEBE-P3G-BBMRI Joint Conference, Brussels/Belgium
25 March 2009	BBMRI 2nd Governance Council Meeting, Brussels/Belgium
20 March 2009	1st Stakeholder Forum, Brussels/Belgium
16 September 2009	Stakeholder Forum Discussion/Information Meeting, Brussels/Belgium
15 December 2009	Stakeholder's Forum Patient Working Group Meeting, Paris/France
16 December 2009	Expert Centre Meeting, Paris/France
9 April 2010	BBMRI meets Mediterranean Biobanks, Valletta/Malta
9 June 2010	2nd Stakeholder Form, Brussels/Belgium
23-25 September 2010	Biobanking for Science Conference, Amsterdam/The Netherlands
26 October 2010	European Parliament Hearing on Health-related Research Infrastructures, Brussels/Belgium

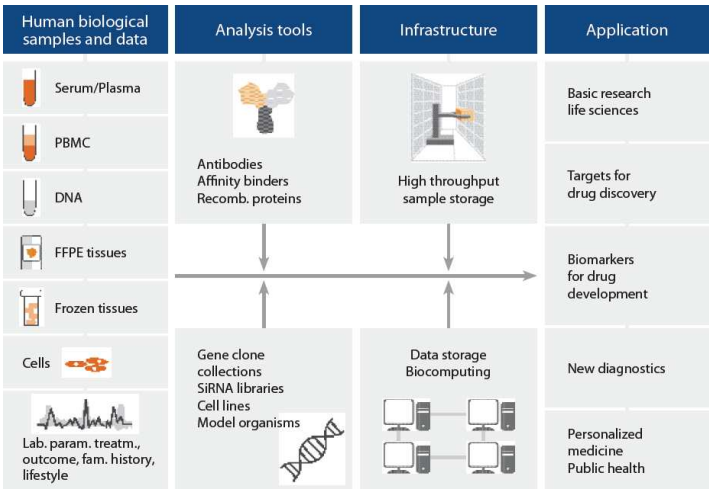
5.2 Components of the infrastructure

BBMRI-ERIC builds on existing sample collections, resources, biobanking technologies, and expertise, which will be specifically complemented with innovative components (Fig. 2). In particular, BBMRI-ERIC comprises

i) all major population-based and clinical-oriented biobanks,
ii) biomolecular resources, such as model and microorganisms, collections of antibodies and other affinity binders and a variety of molecular tools to decipher protein interactions and function,
iii) bio-computing and sample storage infrastructure, including biobanking technologies
iv) scientific, technical as well as ethical and legal expertise.

All resources will be integrated into a pan-European distributed hub-and-spoke structure-like network, and will be properly embedded into European scientific, ethical, legal and societal frameworks. Specific tasks in the planning of BBMRI comprised the preparation of an inventory of existing resources, achieving interoperability by implementation of common standards and access rules, establishment of incentives for resource providers, and to develop solutions for international exchange of biological samples and data which properly consider the heterogeneity of pertinent national legislation and ethical principles.

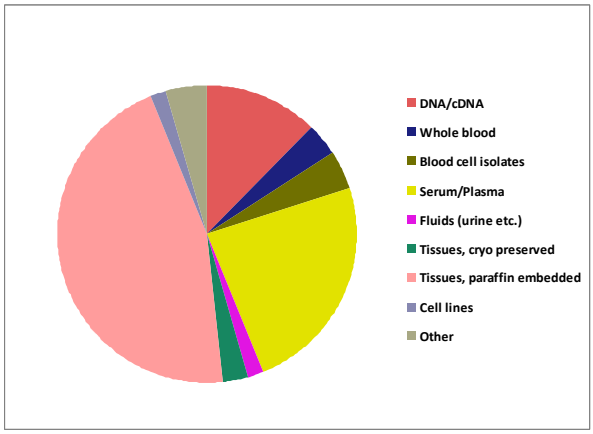
Fig. 2 - Key components of BBMRI-ERIC



Catalogues of European Biobanks

An inventory has been prepared of existing major population-based and clinical or disease-orientated biobanks in Europe (Fig. 3). Based on questionnaires designed in collaboration with the Public Population Project in Genomics (P^3G) information has been collected on type and quality of collected samples and data, standardisation of procedures, IT solutions as well as governance structure, funding, and legal and ethical issues. Data obtained from the survey can be accessed through a searchable catalogue at the BBMRI website (www.bbmri.eu) (Wichmann et al., 2011).

Fig. 3 - Composition of 20 million human biological samples in Europe



Biomolecular Tools and Resources

A review has been performed on existing resources for affinity reagents (Taussig et al., 2007) and other biomolecular resources as analytical tools applicable to biobanking and biomedical research. This led to a new community standard of affinity reagents (MIAPAR) (Bourbeillon et al., 2010), designed to tackle the problems of scattered information and imprecise descriptions and to facilitate database implementation. In addition, a new database for molecular methods including biobanking-related technologies has been established, providing best practice based protocols for processing, preservation and molecular analyses of different types of samples (www.molmeth.org).

Human cell lines

Human established cell lines are widely used to study the mechanisms of tumor development and as preclinical models for tumor diagnosis and therapy, but the chronic problem of cell line cross-contamination has become a major issue. The Cell Line Integrated Molecular Authentication database (CLIMA, http://bioinformatics.istge.it/clima/) has been designed in the frame of the Cell Line data Base (Romano et al., 2009), which currently includes information on more than 6,000 human and animal cell lines available from major European collections. CLIMA represents a unique reference for validated molecular authentication of human cell lines through short tandem repeat (STR) profile.

Database Harmonization and IT-infrastructure

The IT-infrastructure of BBMRI-ERIC will consist of a network using the hub-and-spoke topology to connect the different nodes, which are geographically spread throughout Europe (Muilu et al., 2007). Major nodes act as hubs, and may for instance comprise a specific region or an entire country. Local biobanks constituting the end-nodes will be connected via the national or regional hubs. Information harmonisation will primarily be utilised by a minimum set of data attributes, which are assumed to be achievable from all biobanks. The attributes are defined and standardised according to a controlled vocabulary (for details see Annex II). Use of the system for data discovery will be the first step toward complete data federation. Initially, exchange of source data may be possible by providing appropriate contact information to partners.

Framework for Harmonising Ethical, Legal, and Societal Issues

Optimal access to biological samples and medical data can be provided only if BBMRI-ERIC is built on sound ethics and public acceptance. Analyses of the ethical, legal, and societal issues (ELSI) related to the infrastructure have resulted in the design of i) a coordinated ethical review process ii) a data protection policy for the cross border data transfer issues, both central to the governance of the infrastructure, and iii) in the development of original tools that will facilitate harmonisation. This strategy was based on a conceptual analysis on ethics-related policies for biobanks and biomolecular resources, an analysis of national ethics committee opinions in this domain, and a pilot study (based on research with focus-groups and in cooperation with the 2010 Eurobarometer) on the public perception of biobanks in Europe (Gaskell and Gottweis 2011).
The tools designed consist of a legal Wiki+ platform for disseminating validated existing legal documents in use in EU countries (www.legalpathways.eu), a web based information tool on legal requirements for exchanging biological samples (hSERN; human sample exchange regulation navigator, www.hsern.eu), indicators to promote transparent sharing of biological samples and data and an ELSI transversal platform.
Solutions for secure and efficient trans-national exchange of medical research data is one of the cornerstones for building the European Research Area (ERA) and a knowledge-based economy. For the operation of BBMRI-ERIC various types of data (meta data, pooled data, and object data) will be processed employing Privacy Enhancing Technologies (PETs). Any such approaches will be tested against and based on the common minimum standards set by the European Union for ”the protection of individuals with regard to the processing of personal data and on the free movement of such data”.

Synergies with other ESFRI Biological and Medical Sciences Research Infrastructures

There are currently 13 different biological and medical sciences (BMS) research infrastructures prioritized in the 2nd update of the ESFRI Roadmap in 2010. Most of these infrastructures either require access to human biological samples or rely on biobanking expertise developed within BBMRI-ERIC. Consequently, BBMRI-ERIC will provide direct support of biobanking-related activities for all BMS research infrastructures, particularly for ECRIN and ERINHA (Table 4). At the same time BBMRI-ERIC will benefit from technologies, know-how, and services developed by other infrastructures. For example, BBMRI-ERIC will not establish high-capacity computing and data storage solutions required for dealing with massive genomics, transcriptomics, metabolomics and imaging data derived from human biological samples but collaborate with ELIXIR and the e-Infrastructures on this topic. Furthermore joint grant applications for improving interoperability of data management between BMS research infrastructures have been submitted. The development of coordinated strategies for education and training in the life sciences is already a joint activity of all BMS research infrastructure that is funded by the Innovative Medicines Initiatives.

Table 4 - Synergies of BBMRI-ERIC with ESFRI Infrastructures

BMS RIs	Fields of collaboration
EATRIS	Target identification and biomarkers
ECRIN	Biobanking of clinical samples, ethical and legal issues
ELIXIR	Management of genetic data
EMBRC	Banking of organisms and libraries, molecular tools
EU-OPENSCREEN	Target identification and validation
EuroBioImaging	Identification of imaging biomarkers, diseases phenotype characterization based on imaging data
ERINHA	Establishment of sample collection centres within health care
Infrafrontier	Banking of biological samples, disease phenotype characterization
INSTRUCT	Banking of proteins and gene constructs, NMR-based metabolomics
MIRRI	Biobanking of pathogens
ISBE	Generation of high quality data for computational modeling; correlation with disease phenotype and outcome
Other ESFRI RIs	
ENV	Investigation of gene-environment interactions, documentation of environmental exposure
PSE	Innovative analytical technologies (structural biology)
SSH	Impact of life style and social factors on health; assessment of life style and social factors, data management, privacy
e-Infrastructure	Distributed high capacity data storage and computing

Infrastructures from the Biological and Medical Sciences Thematic Working Group:

- European advanced translational research infrastructure in medicine (EATRIS),
- European clinical research infrastructures network (ECRIN),
- European life science infrastructure for biological information (ELIXIR),
- European marine biological resource centre (EMBRC),
- European infrastructure of open screening platforms for chemical biology (EU-Openscreen),
- European biomedical imaging infrastructure (Euro-Bioimaging),
- European research infrastructure on highly pathogenic agents (ERINHA),
- European infrastructure for phenotyping and archiving of model mammalian genomes (Infrafrontier),
- Integrated structural biology infrastructure for Europe (INSTRUCT),
- Microbial resource research infrastructure (MIRRI)*,
- Infrastructure for systems biology - Europe (ISBE)*.

Infrastructures from other Thematic Working Groups:

- Environmental sciences (ENV),
- Physical sciences and engineering (PSE),
- Social sciences and humanities (SSH).

***** Infrastructures included in the 2nd update of the ESFRI Roadmap.

5.3 Common Requirements for BBMRI-ERIC Partner Biobanks

Biobanks that will become Partners of BBMRI-ERIC have to comply with the principles as defined by the BBMRI-ERIC-Partner Charter (Annex III).The BBMRI-ERIC Partner Charter shall be agreed between national BBMRI-ERIC nodes and the Partners. Participation of a Partner in BBMRI-ERIC is non-exclusive and has no effect on any activity of a Partner outside of BBMRI-ERIC. BBMRI-ERIC acknowledges the primacy of national and European legislation and respects the jurisdiction of competent authorities.

The BBMRI-ERIC Partner Charter requests commitment to implementation of the OECD Best Practice Guidelines for Biological Resource Centres (OECD, 2007), and the OECD Guidelines on Human Biobanks

and Genetic Research Databases (OECD, 2009). These guidelines specify several key requirements of high quality biobanks such as:

The physical biobank facility

The physical biobank facility should be designed to reflect requirements of protecting samples and data from loss, vandalism or theft, implementation of certified processes including sample traceability, protection of privacy of sample/data donors as well as implementation of biosafety and biosecurity measures. According to the biosecurity level of the biological samples handled by a biobank, additional layers of physical security should be provided within the general security area of a facility.

Personnel

A biobank should be led by a senior manager who must be qualified to make sound decisions, particularly on ethical, scientific and managerial issues the establishment proper procedures for the sound operation of the biobank. Responsibilities can be delegated to qualified staff. A biobank should appoint a quality manager who is responsible for administration and monitoring of the quality management system including reporting. Furthermore a biosafety and biosecurity officer should be designated who is responsible that the biobank complies with OECD best practice guidelines on biosecurity.
All staff must have relevant qualification, training and competence in human biological samples and data relevant to the scope of the biobank. All persons having access to a biobank shall be bound by a duty of professional secrecy. Persons with access to confidential data shall be contractually bound to medical secrecy obligations. Rights of access must be managed, traced and limited to authorised persons. All biobank staff shall be briefed regularly and trained in the procedures in effect at the Centre. Training must be duly documented.

Quality management

Procedures should be specified in “standard operation procedures”. Procedures relevant for handling human biological samples must follow the “Laboratory Biosafety Manual” of WHO (the World Health Organisation). Procedures have to be validated and regularly controlled.
Duplication of the collections shall be performed when possible, and stored in separate locations.
Internal and external audits are necessary to monitor quality, and should be performed regularly and duly documented. Biobanks must apply for certification through a process approved by national governments either through a certification body recognised by government or through a transparent certification procedure recognised by government or directly by government agencies.

6. Strengthening European Research

6.1 Contribution to European policies and priorities

BBMRI-ERIC will provide essential resources and technologies of any research-led response to several of Europe's grand challenges, and consequently, will be a fundamental component in addressing the ongoing and future requirements particularly of the EU's health services framework including competitiveness and innovativeness of health-related industries. BBMRI-ERIC will provide an essential research infrastructure to fulfil the goals of the Horizon 2020 framework programme for research and innovation. In particular BBMRI-ERIC should avoid duplication of investments into infrastructure related to biological sample and data management in the upcoming programmes and individual calls of Horizon 2020.

Sustainable health care for ageing populations and personalized medicine

The EU's ageing population is resulting in an increase in certain diseases and consequently in an increased health care expenditure for people in old age that place pressure on the sustainability and viability of the EU's healthcare systems. The ability to better diagnose, treat, and ultimately cure diseases in the 21st century will depend on two things: understanding the genetic and environmental causes of disease, and the ability to translate this information into new diagnostic tests, therapeutics, and preventive measures. Furthermore, future research strategies will place more emphasis on investigation of factors that protect people from developing diseases. Such studies will lay the foundation for science-based approaches towards healthy ageing, and critically rely on biobanks that enable such research.
Clinical practice is shifting from treatment based on symptoms to treatment based on each person's unique genetic make-up and affected biological mechanisms - in other words, personalised medicine. BBMRI-ERIC will provide access to high quality human biological samples related to a broad spectrum of disease as well as medical data, lifestyle and environmental exposure information thereby enabling systematic research as the foundation of future healthcare.

Measures to improve health inequality in Eastern European countries

Access to good quality health services is an important determinant of socioeconomic inequalities in health. The most commonly used definition of 'equitable access to health services' is described as equal access to treatment for those in equal medical need, irrespective of other characteristics, such as income. EU Member States have identified the need to ensure equal access for all as a priority. This goal can only be achieved by targeted investments into health care to address the key factors contributing to inequalities. BBMRI-ERIC will provide the infrastructure for investigation of these key factors by providing solutions for transnational comparative analysis of epidemiology and etiology of diseases, disease outcomes, and the impact of lifestyle and environmental factors. In this context BBMRI-ERIC will play an important role in implementing the Warsaw Declaration's goals of a concerted action to address health inequalities in Eastern European countries that have been agreed by Health Ministers of Eastern European countries under the leadership of Poland.

Contribution to Cohesion Policy and implementing the ERA

BBMRI involved in its preparatory phase more than 270 institutions from more than 30 countries which underlines its pan-European scope. Nevertheless, among the institutions involved there is a significant dominance of Western European Member States. In the context of implementing the European Research Area and European Cohesion Policy BBMRI-ERIC promotes participation of new Member States with its distributed architecture, by the adoption of the ERIC legal framework, and a series of specific stimulation programmes. This process will be officially supported by the Czech Republic. Furthermore, Estonia, Greece, and Malta have expressed their interest in acting as regional hubs for the Baltic, South-Eastern and Southern European regions, respectively, in order to stimulate cooperation within these regions.

Europe's response to pandemics and security threats

New threats to health have emerged, such as pandemics, bioterrorism and physical and biological incidents as well as to solve the problem of climate change and new security threats. BBMRI-ERIC will also establish dedicated sample collection centres for infectious diseases within the health care systems of Member States that will closely collaborate with the European Research Infrastructure for Highly

Pathogenic Agents (ERINHA) guaranteeing that emerging pathogens are rapidly detected and research data can be generated that are required for a proper risk assessment to support fact-based decision making for preventive measures. Furthermore, implementation of biosecurity solutions to prevent dual use of biological materials at biobanks and biological resource centres will be promoted by BBMRI-ERIC. Biosecurity is a highly sensible field that can only be implemented in a European and internationally coordinated effort.

International standards for sample pre-analytics for biomarkers

Investigation of human biological samples has been the central source of our current knowledge on diseases, and laid the foundation for most diagnostic as well as therapeutic opportunities. Modern technologies for the analysis of human biological samples critically rely on defined sample quality. Therefore, standards defining sample quality are directly related to the quality of a diagnostic test (biomarker assays) performed on these samples. Any modification in the regulation related to the quality of human biological samples and consequently also on biomarkers will have an immediate economic and political impact at the international level.

New models for public-private partnerships to support innovation

Exploring new models for public-private partnerships will become a cornerstone for implementing the goals of the Europe 2020 strategy, in particular the “Innovation Union”. BBMRI-ERIC is developing the concept of Expert Centres which can be established as public-private partnerships with industry. These centres should provide a framework where public resources as well as expertise and technologies from academia and industry can be integrated to speed-up collaborative research and to perform analyses of samples at the country of origin under internationally standardised conditions.
A network of Expert Centres that implement common quality assurance schemes, and will be established in association with BBMRI-ERIC and outside of Europe, will create a framework that particularly facilitates international biomarker validation studies. Furthermore, in the context of Expert Centres the role of intellectual property in pre-competitive research will be newly positioned aiming at generating a win-win situation for the public and private sectors and at the same time improving competitiveness.
Expert centres are not operated under BBMRI-ERIC but BBMRI-ERIC will perform accreditation of Experts Centres for being compliant with the criteria developed by BBMRI-ERIC (see 9.2.1.).

6.2 Global integration

International competitive position

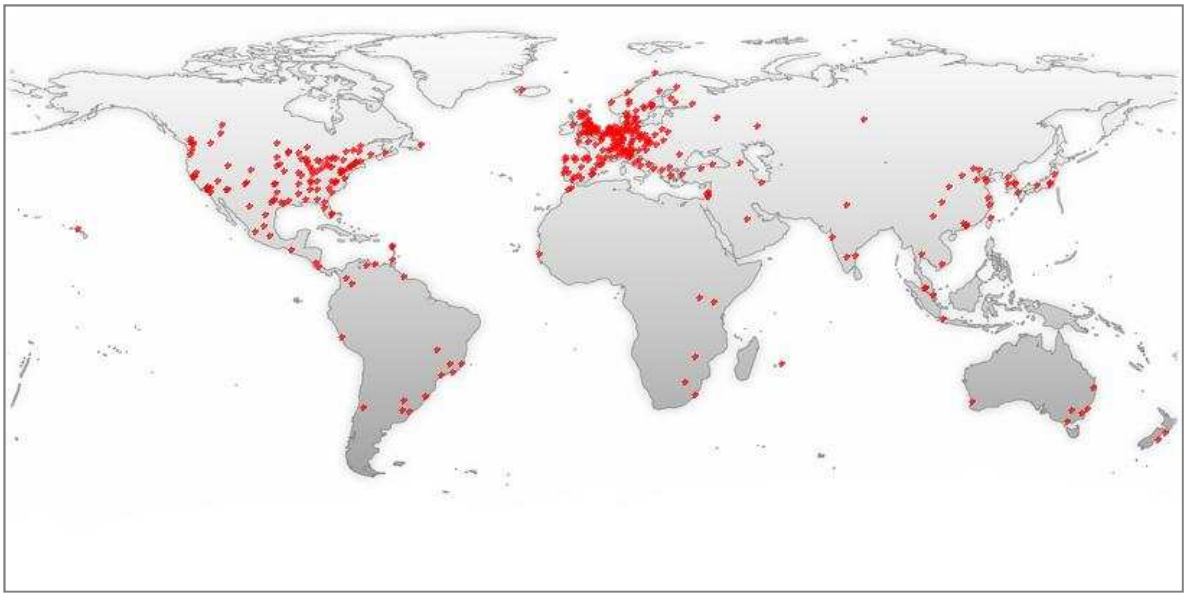
Due to an increase in global competition Europe is losing some ground concerning science and research, especially in the highly competitive field of the life sciences. However, biobanking is a field where Europe is currently in a leading position as demonstrated by the global biobanking landscape (Fig. 4). By far, Europe has the highest number of biobanks as well as biological samples stored within its institutions. By joining forces and collaborating within the BBMRI networking infrastructure Europe will even further develop its leading role and will be highly visible in the global dimension. Since biological samples are considered the key resource for life science research in the future BBMRI will have a positive impact and a stimulating effect on the outcome and the quality of European biomedical research. It may well be that Europe will serve as a model for other regions of the world and thereby enhance its scientific credentials.

International collaboration

The aspects of harmonization of technical, ethical and legal standards for biobanks are global issues (Hewitt, 2010). Therefore, BBMRI-ERIC constantly references its aims and objectives with other international initiatives such as the Public Population Project in Genomics (P^3G), the Innovative Medicines Initiative (IMI), the International Society for Biological and Environmental Repositories (ISBER), the Organisation for Economic Co-operation and Development (OECD) and the World Health Organisation (WHO). BBMRI-ERIC will implement the OECD best practice guidelines for biological resource centres, and consequently will become the European part of the Global Biological Resource Centre Network (GBRCN) (see below). Furthermore, the establishment of an international network of Expert Centres as proposed by BBMRI-ERIC should facilitate international research collaborations by reducing the need for sample shipment and allowing primary data and value generation from biological resources in the country

of origin. Discussions on international collaboration of BBMRI-ERIC have already been initiated with Africa, Canada, China, United Arabian Emirates, and USA,

Fig. 4 - Geographical distribution of scientific publications related to biobanking



Source: Pubmed

BBMRI-ERIC as the European part of the Global Biological Resource Centres Network (GBRCN)

During an OECD workshop in the year 2007 the concept of a GBRCN was discussed and since then pilot projects for a GBRCN of the human as well as of the microbial domain of biological resource centres have been started. Also within this process Europe has so far taken the leading role. It is foreseen that if GBRCN develops further BBMRI-ERIC will build the European branch within this network. In order to prepare for a global integration BBMRI-PP has consciously taken the decision not to define its own European standards but to build upon already existing international standards, the OECD best practice guidelines for biological resource centres.

7. Access to BBMRI-ERIC infrastructure

BBMRI-ERIC will provide access to the sample and data collections of BBMRI-ERIC Partner Biobanks as well as biomolecular resources, expertise and research services.

BBMRI-ERIC shall provide access to samples and related clinical data based on the scientific excellence of the proposed project as determined by an independent peer review and on ethical review of the research project proposal.

BBMRI-ERIC shall provide free access to documents, Standard Operating Procedures (SOP's) and best practices developed by BBMRI-ERIC,

BBMRI-ERIC shall seek to ensure that the source of samples and data be appropriately acknowledged and should request that such attribution be maintained in subsequent use of the samples and data.

Access to human biological samples and identifiable medical data has to be compliant with a variety of ethical and legal requirements, such as the Oviedo Convention (ETS 164), the Helsinki Declaration, the OECD Guidelines for Human Biobanks and Genetic Research Databases (HBGRD) (OECD, 2009), the Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin, and the Directive 95/46/EC on the Protection of Personal Data (examples of relevant legislation and guidelines are provided in Annex IV). Internationally agreed key principles relevant to the operation of BBMRI-ERIC are that research on human biological samples and identifiable medical data require informed consent from the sample and data donor, and approval by an ethical review board. Both HBGRD and the Helsinki Declaration foresee that in case informed consent cannot be obtained for practical or scientific reasons, ethical review boards can provide a waiver for informed consent. Alternatively, anonymization would also waive the requirement for informed consent. Therefore access procedures of BBMRI-ERIC to human biological samples and medical data have to consider the following principles:

- No information related to individuals and their samples can be made freely accessible by internet; only access to coded and aggregated data can be provided through the BBMRI-ERIC web-portal
- Access to samples and medical data can only be provided in the context of a specific research project in accordance with the terms of the consent given by the donor
- The research project has to meet the criteria of scientific excellence (based on scientific review) and has to be approved by a ethical review board
- All procedure have to protect privacy of sample donors

The first step in the access procedure is to register at the BBMRI-ERIC website (

Fig. 5). A web-based query tool will allow obtaining an overview on available samples and associated medical data. The information provided relates to aggregated data that are sufficiently specific to define a research project. In case required samples, data, or resources could be identified, an access fee will be charged for further steps supported by a project manager at the Executive Management Office and the National Coordinators. In coordination with the BBMRI-ERIC Partner biobanks a research proposal will be drafted for scientific and ethical review. The ethical review by BBMRI-ERIC Ethical Review Board (ERB) is obligatory for all projects to obtain access to human biological samples or medical data through BBMRI-ERIC. It does not replace the requirement for ethical review at biobank institutions but should support the local ethical approval committees in their decision making process. This should contribute to the harmonisation of ethical requirements throughout Europe thereby substantially improving efficacy of national/local review processes, particularly in the context of multinational studies. Scientific review by the BBMRI-ERIC Scientific Review Board (SRB) is not required for projects that have already undergone a qualified peer review process (e.g., EU-funded projects or projects funded by national funding agencies). After positive review a Material Transfer Agreement (MTA), specifying the terms of access (e.g., scientific collaboration, cost recovery for local biobanks, intellectual property rights, reporting requirements, and confidentiality) has to be signed between requestor and local biobanks. Intellectual property rights have to be negotiated on a case by case basis depending on the actual contribution of the parties involved to an invention. Providing samples or data per se is not considered as an inventive action and should not warrant co-ownership of intellectual property. However benefit sharing models might be considered as fair mechanism for compensation in case the samples and data provided led to intellectual property and successful products. Furthermore, BBMRI-ERIC recommends that primary data generated by the analysis of human biological samples are made publicly available without protection of intellectual property (see also 9.2.1 Expert Centres). This recommendation does not exclude protection of intellectual property that is based on the analysis of primary data and the conclusions drawn from such analyses. Access has to be compliant with regulations of BBMRI-ERIC Partner biobanks, and Partner biobanks have to decide whether access can be granted for a specific project. This decision has to follow transparent and non-discriminating decision making procedures. Noteworthy, the establishment of high quality research collaboration is the preferred format for access.

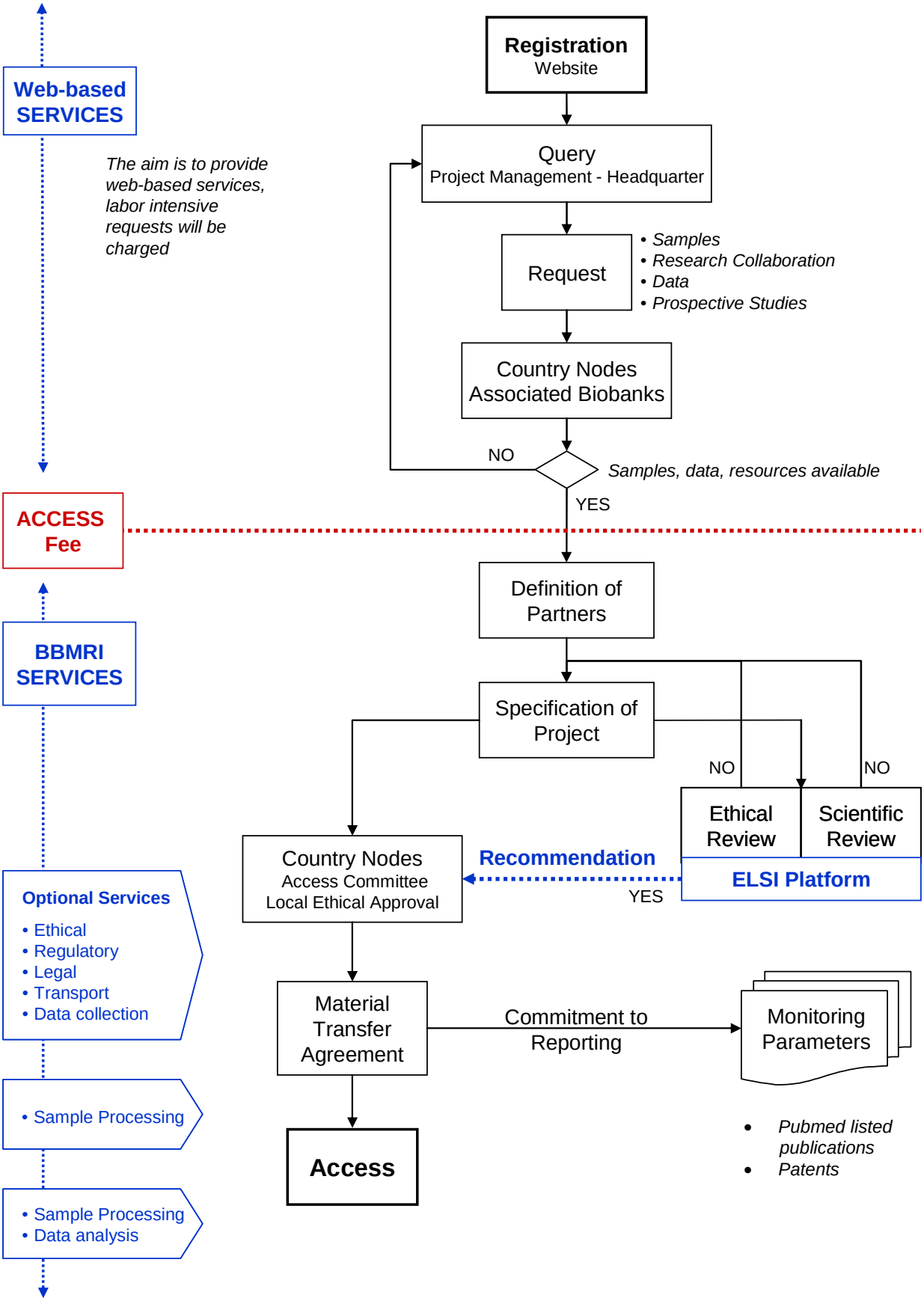
Optional BBMRI-ERIC research services, such as ethical, regulatory, and legal advice, data collection and transportation, sample processing, data analysis, and planning of prospective cohorts can be utilized and have to be agreed on a project by project basis following the same principles as access to samples and data (i.e., scientific excellence as well as ethical and legal compliance). BBMRI-ERIC research services can be agreed as scientific collaboration, as fee-for-service or a combination thereof. Income from BBMRI-ERIC research services will be used to cover operation costs or to further develop BBMRI-ERIC. In case intellectual property is generated by providing research services BBMRI-ERIC will negotiate with the user ownership and exploitation of such intellectual property.
BBMRI-ERIC may also generate intellectual property independent of users by developing technologies for the operation of BBMRI-ERIC. In this case the intellectual property will be owned by BBMRI-ERIC.

Access for industry

There are special issues to be considered for access policies for industrial users. The research in the public domain is based on donations of biological samples, and knowledge and medical data generated thereof are common goods and may not be directly commercialized. The private industry sector on the other hand needs access to biospecimens and data to develop innovative products to keep or gain market leadership. Industry is willing to pay for accessing samples and medical data, particularly when research collaborations are not feasible. However, commercialization of human biological sample and medical data is prohibited in the European Oviedo Convention ETS164 and in national legislation of most Member States. Even financial compensation on a cost-recovery basis that is legally allowed, is generally not accepted by the public (patients, sample donors, patient organizations etc.) or medical professionals not directly benefiting (Biobanks need pharma, Nature 2009). On the other hand high quality samples can't be provided to the industry without any scientific incentives or compensation of the public investments made into building up these resources. This situation is a source of conflict that makes the access for industry difficult or even impossible in many cases. Therefore BBMRI-ERIC developed the concept of Expert Centres that are established outside of BBMRI-ERIC as public-private-partnerships in the pre-competitive, not-for-profit field (for further details see 9.2.1). Expert Centres that are cooperation partners of BBMRI-ERIC will perform the analysis of human biological samples using latest technologies and make the data available to industry to be used in product development. This solution on the one hand reduced the need for direct sample shipment to industry, and, on the other, provides the technical basis that primary data can be efficiently shared and made publicly available as already demonstrated in the context of the Human Genome Project or the Innovative Medicines Initiative. Noteworthy, BBMRI-ERIC-accredited Expert Centres do not replace any existing well working model of academia-industry collaboration but provide a new additional structure to perform research projects that face difficulties under currently established models.

The BBMRI-ERIC access process will be regularly monitored and optimized to reduce time required from posing a specific request to provision of access. BBMRI-ERIC will substantially reduce this time period as compared to the current situation in multinational research projects. The time reduction is a quantifiable performance indicator that directly relates to improved competitiveness of academic and industrial research.

Fig. 5 -Access to human biological samples and associated data



8. Education and Training

Education and Training (E&T) plays a central role in almost all research infrastructure programmes. Within the biobanking domain there is special need for a structured approach towards E&T as currently Europe provides no formal education programmes for biobanking personnel. To better understand the demand for such E&T a questionnaire was developed. 350 of such questionnaires were analysed asking for existing programmes, the need for training and the willingness to participate in such training efforts. 76% are not involved in and have no knowledge of any formal E&T programmes for biobanking. 72% of responders expressed their need for specially trained people of which 83% refer to technician, 55% to personnel at Master level (in life sciences, legal and social sciences) and 50% need personnel at PhD level. 40% of all responders are interested in participating in formal E&T programmes.

One of the objectives of BBMRI preparatory phase was to develop a European Master/PhD curriculum for Biobanking Management. This curriculum is currently tested in Lyon, France, but needs to be spread out over several education centres in Europe. BBMRI-ERIC will play a critical role in establishing and coordinating these programmes. Industry has expressed their high interest in those training activities too. Through the EMTRAIN project of the Innovative Medicines Initiative (IMI) BBMRI is contributing to a new E&T vision for pharmaceutical R&D, especially in biomarker development.

In addition an exchange programme will be implemented for scientists to enhance transnational know-transfer by funding 2-4 month long stays in other centres. Applications to calls of the programme will be peer reviewed and evaluated by a scientific review board. It is intended to apply for additional funding for 'Education and Training' from other sources.

E&T in biobanking is likely to become a European asset for a global market of several thousands of existing biobanks with similar demands in the training of their personnel.

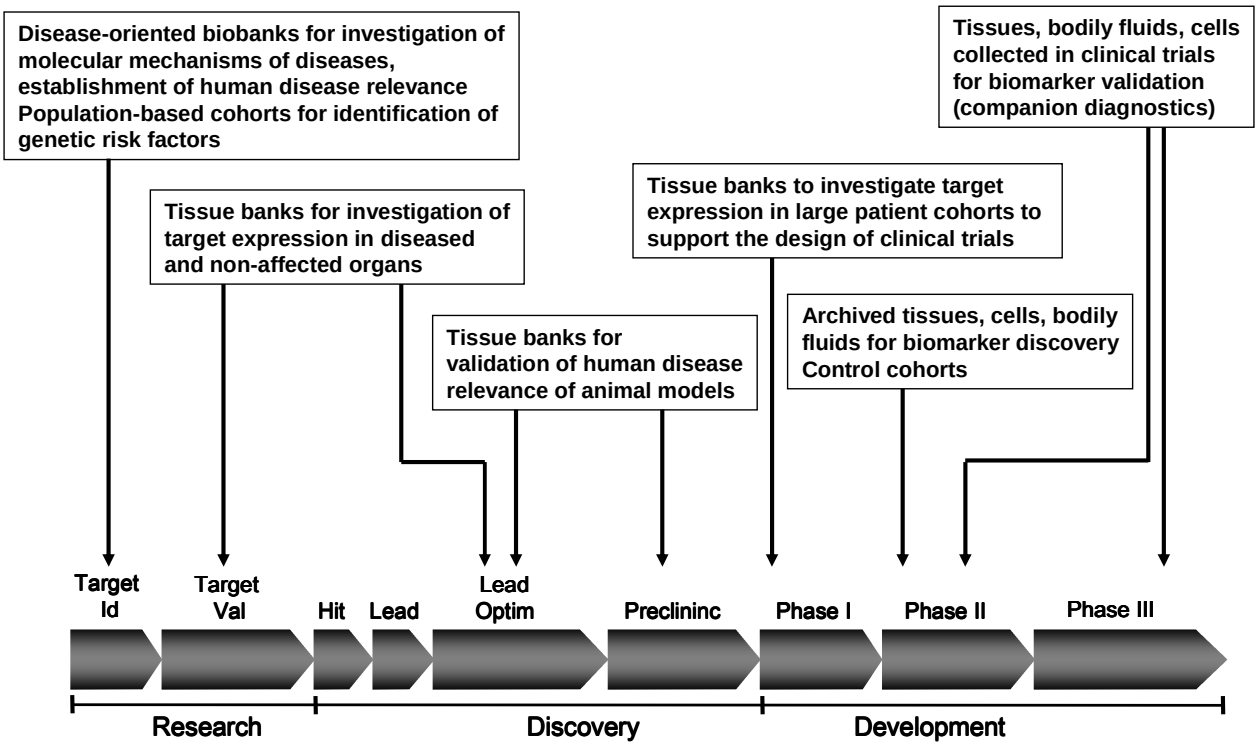
9. Dissemination and exploitation

9.1 BBMRI-ERIC is a resource for pharmaceutical and life science industries

Most of our current knowledge on diseases as well as available diagnostic assays and drugs are based on systematic investigation of human biological samples and medical data. BBMRI-ERIC offers access to a wide and versatile range of biospecimens that are needed in different phases of drug discovery (Zatloukal and Hainaut, 2010) (

Fig. 6). The whole process from the early research stage up to preclinical research and further clinical development can be covered with samples provided by BBMRI-ERIC. Thus BBMRI-ERIC is set up to become a relevant and important source for partners in academic and scientific institutions as well as in the pharmaceutical and life science industries thereby contributing directly to the Innovation Union concept.

Fig. 6 – BBMRI-ERIC offers a wide and versatile range of biospecimens covering the whole drug discovery and development process



Companies working with biospecimens can be categorized into three different groups and include the sectors of pharma and diagnostic industries and biotechnology. BBMRI-ERIC-related markets show significant growth as can be seen by the revenue forecast for the global market of biomarkers with a compound annual growth rate of 18% (Table 5).

Table 5 - Revenue forecast for the global market of biomarkers by segments through 2012 (in $ millions)

Market segment	2005	2006	2007	2012	CAGR % 2007-2012
Biomarker discovery	2.044	2.339	2.677	5.843	1,9
Clinical Trials	450	625	512	1761	23,5
Molecular diagnostics	1.698	1950	2300	5156	17,5
TOTAL	**4.192**	**4.814**	**5.589**	**12.760**	**18**

CAGR: compound annual growth rate
Source: BCC Research, biomarkers report (French ministry of research)

Biotechnology industry market

The number of new so-called biotech firms has increased over the past two decades in all industrial nations. The application areas of biotechnology are quite diverse including therapeutics, diagnostics, chemicals as well as sectors like agriculture, food and cosmetics and the environmental and energy sector. Biotechnology applications are relatively new and are evolving further. There is no single group of homogeneous firms that clearly define the biotechnology industry. One possible alternative is to think about the biotechnology industry in terms of the sectors from which those organizations involved in the overall value added process come. Three segments can be distinguished:

- Universities and research institutes where the underlying bioscience base upon which the technology is created

- Dedicated biotechnology firms which rely on the science base and develop new technological procedures and techniques. This group of companies is dominated by small and medium enterprises which are often started as academic spin-offs.
- Biotechnology commercializing firms which apply the technological procedures of dedicated biotechnology firms to application areas.

BBMRI-ERIC has close links to all three segments which plays an important role for technology transfer activities to be implemented by BBMRI-ERIC (see chapter 9.3).

Pharma & Biomarker market

The global biomarker market is estimated to be $20.5 billion by 2014, growing at a Compound Annual Growth Rate (CAGR) of 19.7% from 2009 to 2014, driven by the high demand for the biomarkers in the field of drug discovery. The markets for biomarker tools and services are expected to grow at a CAGR of 18.5% and 22.2% respectively.
Pharmaceuticals on the market target fewer than 500 human gene products. Even though not all of the 30.000 or so human protein coding genes will have products targetable for drug development, this suggests that there is an enormous untapped pool of human gene-based targets for therapeutic intervention.

Diagnostic industries market

Molecular diagnostics, a new discipline exploiting the '-omics' technologies to classify and understand diseases and to assist individuals at particularly high risk, is currently one of the fastest growing segments in the healthcare industry. This market is being driven by several growth factors, which include optimized sample analysis and data evaluation. Global market size, as measured in terms of dollars, is expected to reach $3.67 billion by 2010 and $6.35 billion by the year 2015.

Biobanking related market

Biobank costumer and supplier companies generate a significant market by themselves and support regional business development. BBMRI creates an incentive for companies to locate within the vicinity of the BBMRI-ERIC partner biobanks and Expert Centres. A lot of important expertise and knowledge in applied sciences is by nature not codified but tacit and will be only transferred by direct contact of involved persons. Physical proximity supports knowledge and technology transfer as is demonstrated by many Biotech Clusters around the world.

The Biobanking related market includes companies in the fields of cryo-technology, reagents, plastic ware (e.g., cryo tubes, vials, cell culture flasks), robotic sample processing systems, reagents and equipment for sample-pre-analytics, sample tracking, biosafety, biosecurity, analytical platforms.

The area of bioinformatics is especially important to biobanks, because bioinformatics based tools are needed to link biospecimens with databases, to analyze data, to set up searchable catalogues, to exchange results. In 2007 the global bioinformatics market was estimated to be about 1.1 € billion.
It is expected to grow at an average annual growth rate of 15.8% to reach nearly $3 billion by 2010, reflecting bioinformatics' explosive growth in pharmacogenomics. The growth of bioinformatics industry, according to experts, can be attributed to its increased usage in the pharmaceutical industry. The application of bioinformatics in drug discovery and development is expected to reduce the annual cost of developing a new drug by 33%, and the time to market for drug discovery by 30%.

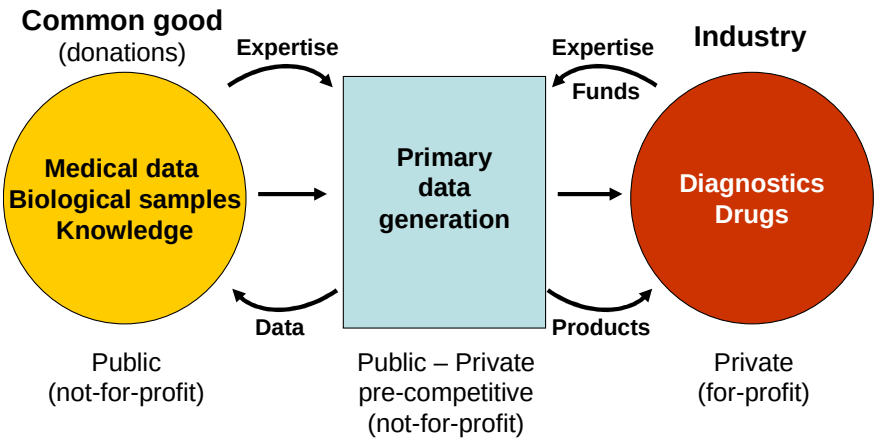
9.2 Dissemination of data and knowledge

9.2.1 BBMRI Expert Centres: The Rationale

Cutting edge research as well as further innovations in the life science industry will strongly depend on transnational access to high quality human biological samples and associated medical information for academia and industry in an efficient and secure manner. Furthermore human biological samples are a finite key resource underlying a series of ethical and legal restrictions thus requiring innovative solutions for efficient usage. By performing the primary analysis of biological samples under internationally standardized conditions in a pre-competitive environment, two major goals are addressed: 1) to provide

access to primary data that can easily be shared in contrast to biological samples and 2) to provide high quality information from biological samples to industry for further product development. This should be achieved by so called 'BBMRI Expert Centres' that are associated with BBMRI-ERIC (Fig. 7).

Fig. 7 - Expert Centres: Collaborative Research of Public and Private Sectors



BBMRI Expert Centres are non-profit organisations that represent a novel public-private partnership model. They are responsible for the analysis of samples in the country of origin under internationally standardised conditions and the generation of primary data. BBMRI Expert Centres integrate pre-competitive public and private research and development activities by providing not only access to biological samples and medical data but also to the broad spectrum of medical and scientific expertise related to the samples, data, and their analysis.

Thus a win-win situation is created for both parties by

- enhancing collaborative research
- using limited resources efficiently
- sharing data, technology, knowledge and expertise
- facilitating innovation
- increasing competitiveness in academic science as well as on the marketplace through product innovation and increased R&D efficacy

Medical expertise

It is becoming more and more important to take into account the whole spectrum of medical, scientific and technological issues related to a certain disease. Important issues are not only the quality of biomolecules extracted from a sample and which features of a disease are actually represented in a biological sample; it is about the whole medical correlation. The entire knowledge about the concerned disease and information on the respective individual are needed to properly interpret the results of an analysis of biological samples.

Technological / analytical expertise and efficacy

The tremendous progress in the development of new analytical technologies resulted in specific sample quality requirements in order to readily exploit the potentials of recent technologies. Therefore it requires specific know-how on sample quality features to guarantee proper interpretation of analytical data generated. This is the more important since evidence-based studies are not available that demonstrate the impact of variations in sample quality on the data generated by various analytical platforms.
Another consequence of the rapid technological advancements is that technology platforms become more and more specialized (e.g., most genome centres have established three or more different next generation sequencing technologies) and major upgrades have to be implemented approximately every 6 months. This situation and the fact that capacities of these new technologies exceed the requirements of most research groups or even whole universities or companies, particularly SMEs, make the case for specialized genome centres that provide research services. Furthermore, there is a need to develop new technologies and statistical tools to integrate and interpret the enormous amount of data generated.

Expert Centres address ethical and legal restrictions

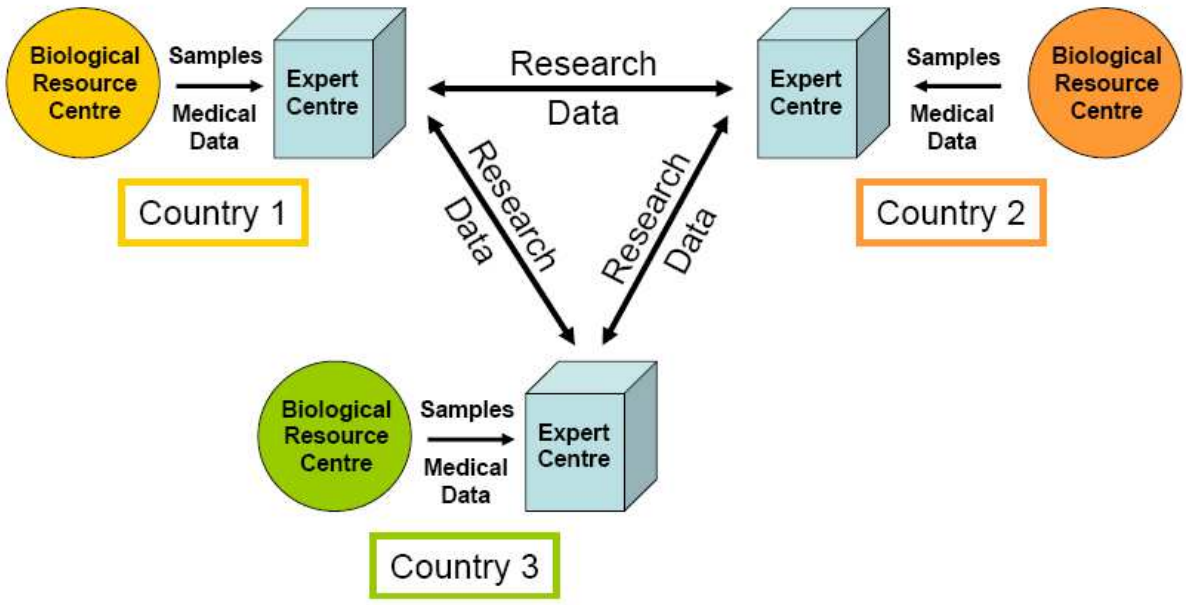
BBMRI Expert Centres function as a focal point of contact between the public and the private sectors. Human biological samples and medical data are provided as donations and are considered as common goods (Fig. 7). The private industry sector needs access to biospecimen and data to develop innovative products to keep or gain market leadership. Since commercialization of human bodily materials is forbidden according to the European Oviedo Convention (ETS 164) and by national legislation in most Member States, and even financial compensation on a cost-recovery basis is generally not accepted by the public, only research collaboration provided a sound basis for accessing human biological samples and associated medical data. This situation is a source of conflict that makes the access for industry difficult or even impossible in many cases. Expert Centres that operate on a not-for–profit basis offer an efficient solution for this problem (see also chapter 1).

Expert Centres as the future "highways" for transnational research collaborations

Several countries like China, Russia, Brazil, India have legal restrictions on export of biological samples that make transnational research collaboration difficult. The establishment of partner Expert Centres in Europe and non-European countries that operate under same standards and quality management schemes could generate novel "highways" for future transnational research collaborations since samples will be analysed in the country of origin and only research data are shared (Fig. 8).

The establishment of a world-wide network of Expert Centres in the context of biobanks and biological resource centres supports the OECD goal to establish a Global Biological Resources Centres Network (GBRCN) in order to provide efficient and secure access to biological samples as key resources for the advancement of biotechnology and medicine. Expert Centres can in addition to public-private - partnerships also be established as public entities.

Fig. 8 - Expert centres as new "highways" for transnational research collaborations



9.2.2 Key features of Expert Centres

Expert Centres are characterised by providing latest technology, adequate IT solutions, cost efficacy, high level of standardisation, professional quality management, confidentiality, flexible solutions for generation of intellectual property, and ethical and legal compliance.

Latest technologies

For optimal biospecimen analysis a wide spectrum of "-omics" analysis platforms needs to be established. Being up to date with the latest developments becomes more and more a technical and financial challenge. Furthermore the tremendous increment of analytical data volume and the necessity to correlate them with clinical and scientific information requires the development of new IT solutions and statistical tools that will be provided by Expert Centres.

Cost efficacy

The enormous advancements in analysis technologies more and more make the case for specialised centres since keeping up to date with this development is neither feasible nor affordable by smaller institutions / non-specialised institutions. These developments are in line with the general tendency of outsourcing specific task to specialised service providers. Furthermore these new technologies, particularly Next Generation Sequencing, do have enormous analytical capacity that can not be properly used by individual institutions. Therefore Expert Centres should operate at lower costs than classical research laboratories in academia and industry.

High level of standardisation

A major limitation in multi-centre studies is that most of the latest "-omics" analysis platforms and the related pre-analytical processes are not sufficiently standardised to allow proper data integration of analysis performed in different centres. This can be improved by implementing harmonized SOPs, common certification and accreditation procedures, use of common reference materials and regular participation in ring trials. Data generated by such internationally harmonised and standardised analysis platforms are expected to be efficiently combined and integrated to investigate a variety of biological and medical questions. This results in a more efficient use of the biological materials analysed and generates important added value for the scientific community.

Professional quality management

Quality management is essential for any industrial research and development, and becomes increasingly important for academic research as well. Quality management within Expert Centres should build on experience established within the industrial field. Appropriate quality management of Expert Centres can be achieved through guidance or supervision by representatives of the industry.

Confidentiality

Any project performed for the industry would underlie strict confidentiality regulations, guaranteeing that no confidential information is disclosed to any other industrial partner or distributed within the academic community. Confidentiality principles will follow the principles as established by Clinical Research Organisations (CRO).

Intellectual property

Providing biological samples or performing analysis on established platforms by itself is not considered as an inventive step and, therefore, does in principle not justify claims on intellectual property by the Expert Centre. However in the context of scientific collaborations joint intellectual property might be generated of industrial partners and Expert Centres. The exploitation of the intellectual property should be as flexible as possible and could be negotiated between the partners on a case by case basis. The general policy should be that industrial partners have optimal freedom to generate value out of intellectual property (e.g., industry as holder/owner of the patents). In case of joint inventions the academic partners should benefit on the basis of royalties or other benefit sharing models that properly consider the contribution of public resources, expertise and work.

Ethical and regulatory issues

Ethical and regulatory issues are often major road blocks to the access to samples and related data. Expert Centres will provide the institutional framework as well as appropriate counselling and services to facilitate ethically and legally compliant access to biological resources for academia and industry within Europe and globally.

Implementation

BBMRI Expert Centres will be established outside of BBMRI-ERIC in the Member countries and have to comply with the following key criteria:

- Involvement of leaders in the field
- Implementation of latest technologies
- Implementation of common quality management systems together with other Expert Centres with similar focus
- Use of common standards & reference samples
- Participation in proficiency testing/ring trials
- Publication of general SOPs for sample pre-analytics, analysis and data generation
- Establishment of confidentiality and IP rules
- Compliance with ethical and legal rules
- Commitment for efficient handling of contracts and projects
- Certification (e.g., ISO)
- Accreditation by BBMRI-ERIC
- periodic external audits by BBMRI-ERIC management

- Cooperation agreement between BBMRI-ERIC and Expert centres that refers to the above mentioned criteria

One of the first activities in establishing Expert Centres will be the definition and provision of common reference samples which is followed by participation in proficiency testing. The results of proficiency test will then guide the strategy for improved interoperability and standardization. The implementation plan foresees to demonstrate the feasibility in pilot studies before major financial commitments can be expected. Some pilot studies are already ongoing. Full implementation should be co- financed from the public and private sectors, and by using funding instruments provided by the European Investment Bank. Major companies have already expressed their interest in BBMRI Expert Centres through their participation in BBMRI Stakeholder Forum and other activities [2] (Table 6).

Table 6 - Pharmaceutical companies and Biotech firms interested in BBMRI-ERIC and Expert Centres

AgileBio	European Diagnosis Manufacturers	Research Center C. Delorme -
Alphelys Lab Technologies	Geneservice Ltd.	Air Liquide
AstraZeneca	GenVault Corporation	RNTech
BioKryo GmbH	Genzyme Corp.	Roche Laboratories
Biomérieux Alliance	Glaxo-Smith Kline	Sanofi-Adventis
Biopharmaceutiques	Imagene	Semmelweis Inno Center
Biostór Ireland	Initial R&D Consulting	Skinethic
BioStorage Technologies GmbH	MacoPharma Laboratory	Steelgate SPRL
Ceiso	Merck	TcLand Expression
CyBioFrance	Modul-Bio	Transgene
Euraccine Consulting	Pfizer	Trans-Hit Biomarkers
		VITRO Ltd.

[2] Participants to BBMRI or to the stakeholder's forum or attendees to stakeholder's meetings or Expert Centres meeting.

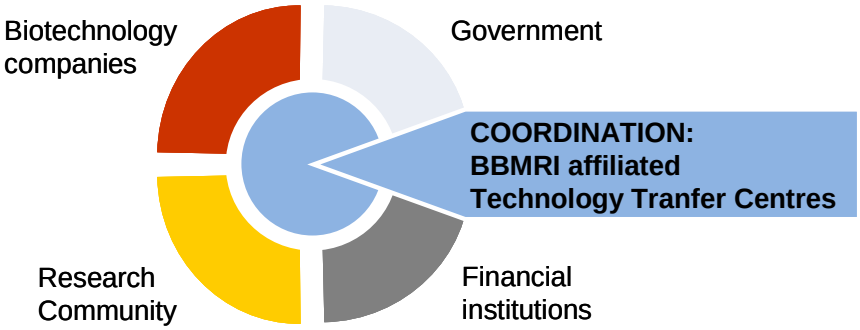
9.3 European Innovation and Knowledge Transfer in Biomedicine

9.3.1 Regional business development

Research institutions and associated infrastructure like biobanks can be the source of innovation and business development of a region. Large companies increasingly rely on outside sources for intellectual property generation. Public funding of research is increasingly linked to technology transfer objectives as the pressure on research public budgets grows because of fiscal deficits. This leads to a fundamental cultural change within research institutes. Exploitation of research results becomes more and more important. These trends represent a great opportunity for BBMRI related technology transfer.

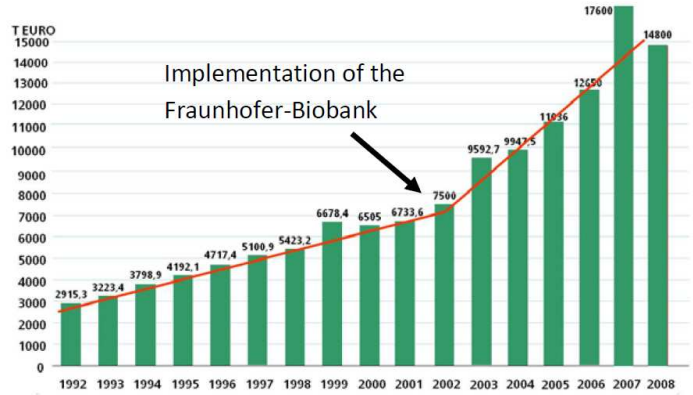
Through coordinated collaboration of research institutions, biotechnology companies and the supply of public and private funding sources geographic concentrations of biobanking related interconnected companies and institutions can be developed. Such clusters foster cooperation and promote competitiveness at the same time (Fig. 9).

Fig. 9 - BBMRI as seed for regional cluster formation with five sets of actors



These effects were observed around San Francisco as well as in Cambridge and are exemplified for a BBMRI related region around the biobank activities of the Fraunhofer Institute for Biomedical Engineering (IBMT) within the Saar region. From its beginning, this institute grew continuously in its budget volume and staff. This growth was only possible by discovering and investing in new areas of interest, like the area of cryotechnology in the year 2002 (Fig. 10). About 31% of this budget is generated with industrial project partners.

Fig. 10 - Development of the IBMT-Budget from 1992 to 2008



In the 'Case Study on the Economic Impact of Biobanks illustrated by EuroCryo Saar' in 2009 shows that a clear impact on the economic development of the Saar region could be assigned to the biobank[3].

- The existence of the biobank enabled several major R&D projects.

[3] http://www.bbmri.eu/index.php/publications-a-reports

- The operational budget of the division Biophysics and Cryo-technology, one the main users of the Fraunhofer Bioarchive, grew from 200 T € in the year 2001 up to 3.5 million € in the year 2009.
- Biobank activities resulted in job creation within the biobank itself and in connected R&D groups.
- Based on basic research in cryo-technology three science based spin-off companies were recently founded and further concepts for spin-offs are being evaluated.
- So far, more than 20 patents of the Fraunhofer cryo-technology-family are licensed to companies.

Taken together, the observed positive development resulted in additional 12 million € of public funding for further development of the biobank infrastructure within the next three years.

9.3.2 Pan-European exploitation initiative

An enormous potential exists in Europe for biomedical innovation and knowledge-generation and transfer based on the population base of more than 500 million citizens, a sophisticated medical-clinical infrastructure, and an advanced biomedical research community that has become highly integrated as a consequence of EC initiatives (e.g. FP, ESFRI programs), as highlighted by the Commission's "European Innovation Union" concept. These resources could be leveraged into an enhanced generation of economical and health-care progress by embedding them into collaborative European networks with a clear orientation towards the value-chain ultimately focused on products and services.

Building on BBMRI-ERIC, we propose to create a European effort and associated infrastructure to coordinate and foster cooperative efforts that integrate extant biological repository resources (as established by BBMRI) and advanced basic and applied biomedical research resources in both academia and industry, with an clear focus towards novel therapeutics and diagnostics as well as new public health initiatives. It is envisioned that these efforts will specifically include the Eastern and Central European countries which have recognized a clear need in this regard ("Warsaw Declaration"). Moreover, they will be internationally networked beyond the EC (US HHS/NIH, OECD) to leverage the European position in a global context.

9.3.2.1 Structure of BBMRI associated Technology Transfer Centres

We envision a "distributed hub-and-spokes" structure with national or regional coordinating technology transfer centres for Western, Southern, and Eastern/Central Europe which will ensure regional as well as pan-European coordination. Utilizing and expanding on extant BBMRI-based infrastructure, the network will foster access to relevant bio-repositories as a central resource for collaborative research programs that formulate clear and specific deliverables along a mapped value-chain.

BBMRI-ERIC Partners and Expert Centres offer infrastructure and the latest technology at a quality level that companies would not be able to set-up for themselves on a permanent basis. Not only large corporations benefit from BBMRI-ERIC but also SMEs (small and medium enterprises) which enhance their competitiveness through BBMRI-ERIC supported fast and efficient sample analysis as required by a variety of biotechnology and pharmaceutical companies, particularly in the fields of biomarker and drug research and development.

As demonstrated in the Saar region the existing biobanking infrastructure and expertise offer the potential to

- enhance collaborative research
- create jobs
- facilitate innovation
- enhance patent licensing
- be the source for spin-off companies
- to increase the competitiveness of companies
- to support knowledge and technology transfer
- to become an interesting industry location and to attract companies

These efforts have to be coordinated in an efficient and structured manner by BBMRI associated Technology Transfer Centres.

9.3.2.2 European Investment Bank Funding Instruments

Technology Transfer is one of the strategic areas of the European Invest Bank (EIB) which has a strong technology and industry expertise in the sector of life sciences. The EIB seeks to support through the European Investment Fund (EIF) financially sustainable technology transfer structures.

We intend to develop and set-up an appropriate technology transfer model for BBMRI-ERIC including

- intellectual property generation, licensing and IP portfolio management
- business development
- business incubation services for spin-off companies
- Mezzanine and venture capital funding.

BBMRI-ERIC-associated Technology Transfer Centres should use the expertise and capital from the EIF as well as other funds.

10. Legal Entity and Governance

10.1 The ERIC legal entity

A key task and challenge for BBMRI-ERIC is to provide access to biological samples and data that properly represent the diversity of European populations and diseases. This can only be achieved by a distributed research infrastructure with operational units in most, if not all, European Member States.

The European Research Infrastructure Consortium BBMRI-ERIC

The European Research Infrastructure Consortium (ERIC) legal entity has been identified as the most appropriate legal entity to support the distributed operation of the BBMRI.

BBMRI-ERIC is established for an unlimited period under the Council Regulation (EC) No 723/2009 of 25 June 2009 on the Community legal framework for an ERIC. The ERIC is set up to sustainably establish and operate, on a non-economic basis, the distributed pan-European Research infrastructure “Biobanking and Biomolecular Research Infrastructure, European Research Infrastructure Consortium” (BBMRI-ERIC).

BBMRI-ERIC foresees a Central Executive Management Office in one Member State that coordinates the interaction of National Nodes established in several Member States. The Central Executive Management Office provides a common access portal to resources available in Member States as well as appropriate facilities and expertise. The National Nodes are also established under the ERIC legal entity and link the national scientific community (e.g., universities, hospitals, research institutions, and resource centres) to BBMRI-ERIC. Financial commitment of Members to the establishment and operation of BBMRI-ERIC is initially for a period of three years. An evaluation of BBMRI-ERIC’s activities will be undertaken during this initial period of operation by an independent body as defined by the Assembly of Members.

BBMRI-ERIC will operate under Statutes approved by the Member States and under Rules of Procedure approved by the Assembly of Members.

Legal agreements

BBMRI-ERIC will have the following legal agreements regulating its activities:

- Participating Members States will agree on and sign *BBMRI-ERIC Statutes* to set up BBMRI-ERIC.
- Each biobank will sign the *BBMRI-ERIC Partner Charter* with its National Node to participate in BBMRI-ERIC activities and become a Biobank partner.
- *Services Contracts* and *Material Transfer Agreements* (drafted with support from the Central Executive Management Office and National Nodes).

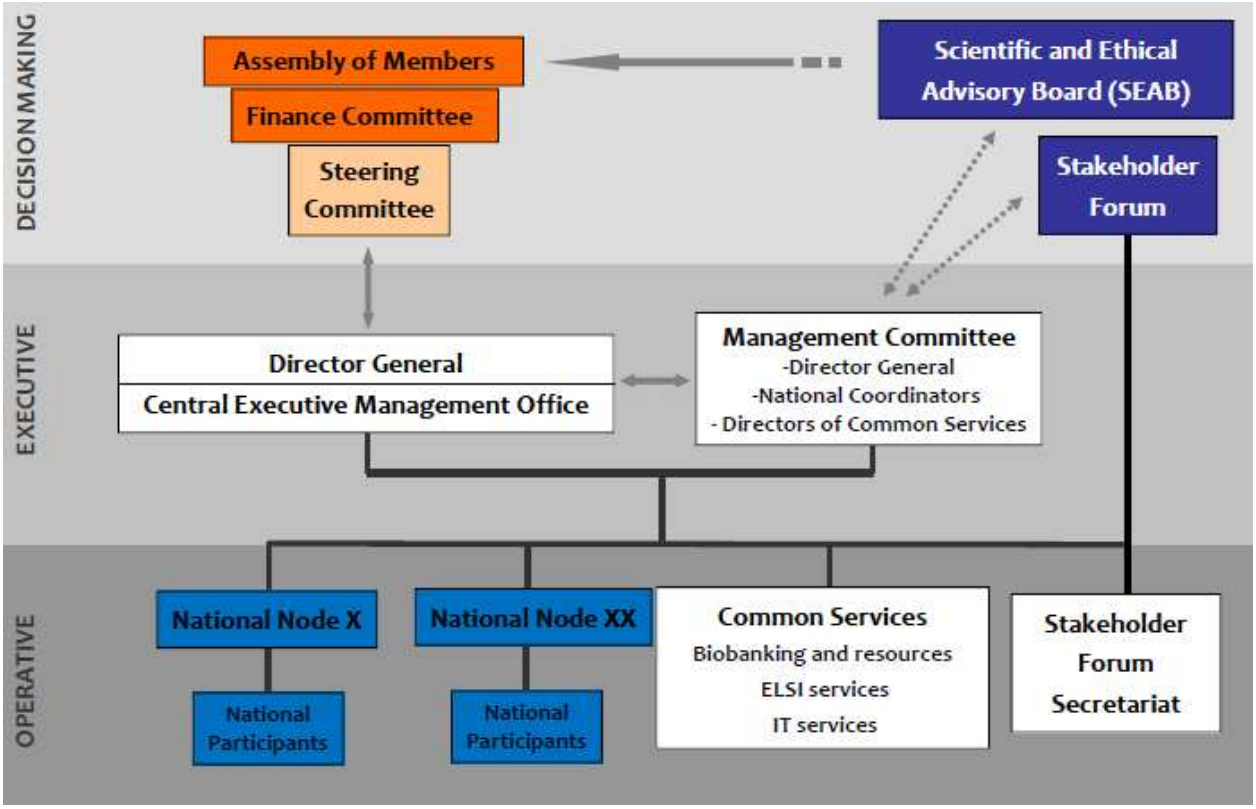
10.2 Governance

The principles of governance and management rules required for operation of BBMRI-ERIC are defined in BBMRI-ERIC Statutes and in the Rules of Procedure adopted by the Assembly of Members in its first session. Fig. 11 illustrates graphically the Governance and Management Structure of BBMRI-ERIC. The Statutes have been drafted in a manner to allow the decision making body, the Assembly of Members and the Director General (the Chief Executive Officer and legal representative of BBMRI-ERIC) to establish such subordinate governance bodies and management structures as deemed necessary when the infrastructure grows and develops without having to make changes in the Statutes.

Members of the BBMRI-ERIC

The Members of the BBMRI-ERIC are the Countries (Member States of the European Union, associated countries and third countries in accordance with Regulation n°723/2009) and intergovernmental organizations that have signed the BBMRI-ERIC Statutes.

Fig. 11 - BBMRI-ERIC governance structure



The white boxes indicate facilities established under the ERIC legal framework.

Observers of BBMRI-ERIC

Countries (Member States of the European Union, associated countries and third countries as defined by the Regulation n°723/2009) and intergovernmental or ganizations can participate to activities of the BBMRI-ERIC as Observers. The status of an Observer is for a maximum period of three years. Observers do not have a right to vote and they pay 30% of their full membership contribution.

10.2.1 Assembly of Members

The Assembly of Members will consist of officially appointed delegates of participating Members (Countries and intergovernmental organizations). Ideally the two-member delegations would consist of one scientific and one administrative delegate. Members may additionally appoint up to three advisors who may serve as proxies to the delegates. The Assembly of Members will be the means by which the Members will make collective decisions on matters relating to BBMRI-ERIC, which will then be implemented by the Director General together with the staff of the Central Executive Management Office and the BBMRI-ERIC Management Committee.

The Assembly of Members shall establish a **Finance Committee** as a preparatory and advisory body to the Assembly. Its responsibilities are to advise the Assembly of Members and the Director General on matters relating to the preparation and management of the budget of the BBMRI-ERIC, its expenditure and accounts, and its future financial planning. The Finance Committee shall submit a proposal concerning the appointment of external auditors to the Assembly of Members. Typically the administrative delegates of the Assembly of Members would form the Finance Committee.

The Assembly of Members shall establish a **Scientific and Ethical Advisory Board** (SEAB) and by two-thirds majority any other subordinate bodies as may prove necessary. The decision to establish such bodies shall include provisions concerning the membership, its rotation and terms of reference. The advisory bodies shall agree on their Rules of Procedure. The task of the **SEAB** is to perform periodical evaluations of BBMRI-ERIC and its different activities. The SEAB shall be composed of distinguished scientists or experts appointed in their own right, not as representatives of Member States. SEAB shall

also advise the Assembly of Members with regard to proposals of the Director General on the realization of the Work Program. The SEAB gives advice to BBMRI-ERIC, but its members are not legally part of it.

The Assembly of Members may also establish by two-thirds majority any other subordinate bodies as may prove necessary. An example of such subordinate body is a **Steering Committee** comprising the Chairs and Vice-Chairs of the Assembly of Members and Finance Committee. The Steering Committee would be responsible for supporting and monitoring the performance of the executive management between the sessions of the Assembly of Members in implementing the decisions of the Assembly of Members, including the Strategic Plan, the Work Programme and the budget, and shall report thereof to the Assembly of Members.

10.2.2 Management of BBMRI-ERIC

The Executive Management of BBMRI-ERIC comprises the **Director General** and the **Management Committee**. Together they plan and oversee all scientific and service activities of the BBMRI-ERIC.

The **Director General** will act as the Chief Executive Officer and legal representative of BBMRI-ERIC following the guidance given by the Assembly of Members, the Governance Board, the Finance Committee and the Steering Committee, if established. She/he shall establish and chair the BBMRI-ERIC Management Committee and shall be responsible to the Assembly of Members for efficient administration of the BBMRI-ERIC and its finances and for ensuring the execution of the decisions of the Assembly of Members and the Governance Board. The Director General shall be assisted by such scientific, technical, administrative and secretarial staff as is authorised by the Assembly of Members. The Central Executive Management Office (BBMRI-ERIC Headquarter) will provide a common access portal to resources available in Member States as well as appropriate services, facilities and expertise.

The **Management Committee** shall be established by the Director General, and comprises high level staff of the Central Executive Management Office, Directors of BBMRI-ERIC National/Organizational Nodes (National/Organizational Coordinators) and Directors of Common Services. The Management Committee may nominate by election from its members a vice chair to help and support the Director General in performing his/her duties. The major role of the management committee is to develop the Work Programme and to support its execution by coordinating the interactions of the key elements of BBMRI-ERIC and the national scientific communities.

A **National Node** is an entity, not necessarily of legal capacity, designated by a Member State, that coordinates the national Biobanks and Biomolecular Resources (e.g., universities, hospitals, research institutions and resource centres), and links national activities with the pan-European and international activities of BBMRI-ERIC . Each National Node has a Director (National Coordinator), appointed by an appropriate authority of the Member State. Each Member (Country) shall establish one National Node.

An **Organizational Node** is equivalent to a National Node in an intergovernmental organization which is a Member of BBMRI-ERIC. An Organizational Node coordinates Biobank(s) and Biolmolecular Resources of the organization, and links its activities with those of BBMRI-ERIC.

Each **Common Service** is managed by a Director, appointed by the Director General after consultation with the national delegates of the Member State where the Common Service is located (and financially supported by the Member State). Common Services are set up in host Member States to establish and support common thematic services. Except for the investments made by the host country, Common Services are part of BBMRI-ERIC.

10.2.3 Scientific and Ethical Review Boards

The following expert bodies, envisaged to be established by the Assembly of Members of BBMRI-ERIC on the proposal of the Director General and the Management Committee, shall function in an advisory capacity to the Director General, the Management Committee and the BBMRI-ERIC National Nodes:

- The **Scientific Review Board**, responsible for scientific evaluation of access requests received by BBMRI-ERIC, and
- The **Ethical Review Board,** responsible for ethical evaluation of requests received by BBMRI-ERIC.

Although members of the Scientific Review Board and the Ethical Review Board give advice to BBMRI-ERIC, they are not part of BBMRI-ERIC legal entity.

10.2.4 Stakeholder Forum (SF)

The Director General will organize a Stakeholder Forum that will consist of senior leaders and experts from relevant parts of the international health and scientific systems to provide feedback and early advice from the broad stakeholder community of BBMRI-ERIC (industrial partners, user community and patient organizations) to the Management Committee and the Director General in relation to the activities of BBMRI-ERIC. The Director General shall nominate members of SF, and decide on its practical organization and on its terms of reference. To ensure sustainable coordination of SF activities a SF Secretariat shall be established under BBMRI-ERIC.

10.3 Organization, tasks and requirements

BBMRI-ERIC will have a lean management based on a Hub and Spoke model to carry out all tasks establishing and operating the European Research Infrastructure. It will be headed by a Director General who will be appointed by the Assembly of Members.

10.3.1 Central Executive Management Office

The Director General will serve as the Chief Executive Officer of BBMRI-ERIC responsible for the Executive Management of BBMRI-ERIC and will be assisted in his managerial functions by the Central Executive Management Office and the Management Committee.

The Executive Management is responsible for:

- Drafting and implementing the Work Programme;
- Overall coordination of the activities of the BBMRI-ERIC National Nodes and Common Services;
- Maintenance of the central user interface, the searchable Web-based overview portal with a catalogue of existing biobank collections;
- Scientific and ethical evaluation of research projects submitted by users in coordination with the Scientific Review Board and the Ethical Review Board;
- Managing all legal issues and contracts with National Nodes, biobanks and third parties;
- Sustaining communication with all relevant stakeholders, including all reporting duties of BBMRI-ERIC;
- Running the budget, accounting and clearance management;
- Fundraising activities (following national and international funding schemes and participation in applications and grant proposals).

Table 7 - Central Executive Management Office Personnel

Function	Job profile
Director General	MD or Ph.D. with international reputation and strong research background, previous research management experience in academia or industry in international context, contract for a defined period of time
Administrative Director	Legal or business background with strong practical experience in finance and controlling, responsible for budget, accounting and clearance management
Lawyer	Lawyer with international law degree with international experience in the area of medical research, responsible for the management of all legal issues and contracts with National Nodes, biobanks, and third parties
IT/Data Protection	Senior IT expert, responsible for IT strategy and core IT competencies in the Headquarter, develops processes and guidelines in accordance with IT Common Services
Quality Manager	Senior quality management expert with previous experience in networking and coordination of national activities based on OECD best practices guidelines, accreditation and certification, responsible for support of biobanks to implement quality standards, set up of BBMRI internal auditing process
Project manager	MD or Ph.D. with scientific research background, management of projects, access to samples, data, initiation and coordination of research collaborations and grant proposals
Project Management Assistant	Scientific academic degree required, support of Project Management, capacity building with increasing number of BBMRI Members
Secretary	Non-academic position, office management and administration

Personnel

- The Director General is expected to have a strong research background in a relevant scientific field. He/she must also have experience in research management in international context.
- The Director General is assisted at the Central Executive Management Office by such staff as deemed necessary by the Assembly of Members. The Assembly of Members shall approve the staff establishment prepared by the Director General and decide on their qualifications as part of the Work Programme. Initially it is envisaged that the personnel as shown in Table 7 will be hired for the Central Executive Management Office.

10.3.2 BBMRI-ERIC National/Organizational Nodes

Placed under the responsibility of a Director (National/Organizational Coordinator) in each participating Country/intergovernmental organization, the National/Organizational Node of each Member forms an interface with national and/or organizational Network(s) of Biobanks and Biological resources and coordinates their activities with those of the pan-European infrastructure, BBMRI-ERIC.

National/Organizational Nodes are responsible for:

- Interfacing BBMRI-ERIC with national, regional or organizational network(s) of biobanks within each Member;
- Administrating databases for national, regional or organizational networks of biobanks;
- Implementation of standards and quality control;
- Processing research projects with dedicated project managers. This includes the management of any additional scientific peer-review or ethical review of proposals if required by local authorities or guidelines;
- Allocating user requests to the national/organizational biobank partners of BBMRI-ERIC;
- Regulatory and legal weavers necessary for transnational exchange of samples and data;
- Overseeing internal and external training activities for biobanking.

Personnel

- The Director of National/Organizational Node (National/Organizational Coordinator) is appointed by the appropriate authority of the Member. He/she participates in the BBMRI-ERIC Management Committee. Since the National/Organizational Coordinator interfaces with national or regional network(s), it is recommended that she/he has relevant research and administrative experience from international biobanking activities. Member States and intergovernmental organizations are expected to provide such support staff for the National/Organizational Node that is deemed necessary.
- BBMRI-ERIC National/Organizational Nodes may organize their activities depending on national or organizational solutions for biobanks and biomolecular resources.

For financial planning the following personnel is assumed to be needed in the National/Organizational Nodes (Table 8).

Table 8 – National/Organizational Node personnel

Function	Job profile
Director	Senior level position, scientific background and practical experience in biobanking
Secretary	Administrative support
Additional Personnel (optional, country dependent)	Project manager with academic degree

10.3.3 Common Services

BBMRI-ERIC Common Services form a key element of the infrastructure as they provide to the biobanking community and biobank users top-levels expertise, services and tools in specific areas of biobanking. Common Services are placed under the responsibility of the Director General and managed by a Director jointly appointed by the Director General and the host Member State where the Common Service is located. It is envisaged that Common Services are jointly funded by BBMRI-ERIC and the Member State hosting the facility. On behalf of BBMRI-ERIC such funding decisions are made by the Assembly of Members on the basis of scientific excellence and cost efficacy as part of the Work Programme jointly funded by the Members. The following Common Services are envisaged for BBMRI-ERIC:

10.3.3.1 Common Biobanking and Resources Services

Common Biobanking and Resource Services should guarantee that procedures and standards for different types of population-based, clinical-oriented biobanks and biomolecular resources are regularly updated according to the developments of the fields and new user requirements. The services will steadily improve interoperability of biobanks located in different BBMRI-ERIC Members, and thereby critically contribute to the quality and overall efficacy of the infrastructure.

The implementation of Common Biobanking Related Research Services requires the following personnel (Table 9).

Table 9 - Common Biobanking and Resources Services Personnel

Function	Job profile
Director	Senior level position, scientific background und practical experience in biobanking
Secretary	Administrative support
Assistant	Project manager with academic degree

10.3.3.2 Common Information Technology (IT) Services

A key role of BBMRI-ERIC is to coordinate and implement the interoperability of the existing and new biological databases of biobanks. The IT-infrastructure of BBMRI-ERIC will consist of a network based on the hub-and-spoke topology to connect the different nodes, which are geographically spread through Europe (Muilu et al., 2007). Local biobanks constituting the end-nodes will be connected via the national or regional hubs.

Both centralized and national IT services are needed to achieve database management and IT interoperability within BBMRI-ERIC. Common IT Services will connect the entire network of National Nodes, Common Services, individual biobanks, users and observers into a single virtual structure, preserving on one hand privacy and autonomy, and supporting communication and collaboration on the other hand. Considering the central role of IT services each National Node should nominate an IT representative to support this process (for details see Annex II).

The composition of the staff of the Common Information Technology Services is summarized in Table 10.

Table 10 - Common Information Technology Services Personnel

Function	Job profile
Head of Informatics	Ph.D. in medical or bioinformatics, several years of responsibility for big projects between European countries, responsible for harmonization and set up of the hub and spokes structure
Systems architect	Senior level position, informatics degree or many years of experience from the industry and practical experience with Agile software development required, responsible for the design of IT layers (interface to users, connection of user hub and spoke, etc.).
Programmer	Experience with system programming (JAVA) and database programming which is required for the programming of the central parts of the connected Hubs.
Developer	The main task will be to construct and maintain the web-portal, which will be the user interface, in addition responsible for the biobank lexicon to be implemented in many European languages
ICT Support Manager	A support centre for ICT biobank activities and updates for the disclosure filters
Administrative support	Office management and administration

10.3.3.3 Common Technology and Reagent Services

The BBMRI-ERIC will have as an important function to ensure broad access to state of the art and beyond state of the art techniques and reagents for biospecimen analysis, and to promote interoperability of data across studies and biobanks. A network will be established and continuously updated, linking centres across Europe that provide access to relevant technologies for measuring and imaging nucleic acids, proteins, metabolites, etc.. By ensuring that advanced, in some cases unique emerging methods, are put to early and efficient use with high-quality biobanked samples, scientific progress as well as commercial application by biotech, diagnostic and pharma industries will be promoted. Expected commercial effects include new disease biomarkers, drug targets, molecular technologies, besides generally improved understanding of disease mechanisms. Examples of functions that will be provided include the following:

- Continuous identification and cataloguing of service providers for biobank analyses
- Provision of guidance for the collection and storage samples to meet requirements of analytical technologies
- Provision of guidance about biobanking technologies
- Maintenance of catalogues of detection reagents, and of molecular technologies
- Ensuring broad access to resources of reagents, e.g. antibodies, for sample analysis, and cell lines'
- Contributing to the establishment of procedures for documenting and standardizing assay techniques
- Supporting efforts to enhance interoperability of data across studies and biobanks
- Provision of information on emerging assay techniques on the horizon
- Promotion of development of new methods that can strengthen biobank research

Table 11 - Common Technology and Reagent Services Personnel

Function	Job profile
Head of technologies and reagents services	Ph.D. in medicine or biology. Advanced scientist with expertise in molecular technologies and reagents.
Coordinator of technologies and reagents services	Ph.D. in medicine or biology. Experience from large-scale biobanking and application in academia and/or industry.
Database developer	Ph.D. in medicine or biology. Advanced skills in building databases and coordinating with molecular technologists and users.
Programmer	Experience of systems programming and developing interactive, user-friendly databases. Some familiarity with molecular biology desired.

10.3.3.4 Common Service for Quality Management

The quality management Common Service will:

- Define quality management criteria and oversee their implementation in biobanks;
- Seek to harmonize and standardize Standard Operating Procedures (SOPs) and disseminate them;
- Advice biobanks on quality requirements of industry users
- Set up training in quality control for biobanks;
- Advice in certification of biobanks;
- Audit quality management when requested;
- Perform accreditation of Expert Centres.

The Quality Management personnel will be employed directly in the Central Executive Management Office (Table 7).

10.3.3.5 Common Service for Ethical, Legal and Societal Issues

For efficient running of the ELSI Common Services each National Node is expected to designate a National ELSI Representative to participate in the ELSI Common Service activities and to interface with National Institutions, Biobanks and BBMRI-ERIC. The ELSI Common Services will provide a Platform to:

- Maintain a "Hot Line" to respond to ethical issues raised by users as well as an HSERN platform that provides access to existing ethical and legal frameworks for the exchange of human biological samples for research use in Europe.
- Ensure the dissemination of results of surveys conducted toward various audiences (patients, donors etc.)
- Set up training for biobanks managers and ethics and legal officers.
- Initiate a pioneer and interactive approach and tool to address the complex legal issues associated with pan-European biobanking: The Wiki Legal Platform. The Wiki is to provide a dynamic, online, grass roots platform for sharing, discussing, validating and issuing authoritative and reliable legal forms and standards.

Table 12 - ELSI Common Services Personnel

Function	Job profile
Chair of Research Ethics Committee	Senior level position, MD or Ph.D. with international track record in ethics in medical research
Lawyer	Lawyer with profound knowledge in the areas of data protection and with compatibility of national legislation within BBMRI-ERIC member states
Secretary	Office management and administrative support

10.3.4 Stakeholder Forum Secretariat

A key indicator to the success of BBMRI-ERIC will be the ability to form direct relationships with stakeholders. (patient organisations, industry representatives, user community, medical societies and other health-related organizations, and research infrastructures). The Stakeholder Forum Secretariat will provide recommendations to the Assembly of Members and Director General on all matters of direct or indirect interest to stakeholders in relation to biobanking and biomolecular resources For the coordination of Stakeholder Forum activities, a Secretariat should be established requiring the following.

Table 13 - Stakeholder Forum Secretariat Personnel

Function	Job profile
Manager	Executive Manager, MD or Ph.D. with scientific background and experience in biobanking, good networking capabilities, establishment of connections to pharmaceutical industry and patients' associations
Secretary	Administrative support

11. Implementation plan

Setting up the BBMRI-ERIC will require a series of steps following the BBMRI preparatory phase. As already mentioned in chapter 5 the BBMRI preparatory phase lasted from February 2008 to January 2011 and was funded by the European Commission via the 7th framework programme. The aim of the preparatory phase was to define the legal and governance structure of the BBMRI infrastructure, to describe the technical and operational framework and to come up with a sustainable funding model. With the finalization of the draft documents to apply for the BBMRI-ERIC the goals of the preparatory phase are achieved.

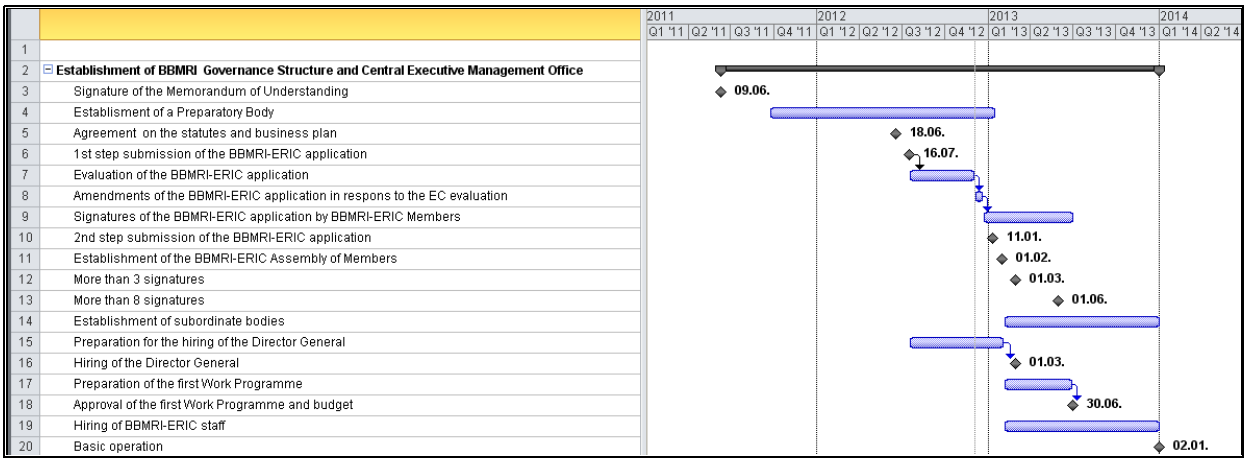
In order not to lose the momentum of the preparatory phase and to guarantee a continuous transition towards the implementation of BBMRI-ERIC a series of steps how to proceed have been identified. These steps comprise the following (summarized in Fig. 12):

Those countries that have signed a Memorandum of Understanding (MoU; Annex V) will respond to possible requests of the Commission in the context of the evaluation of the BBMRI-ERIC application and to support the implementation of BBMRI-ERIC until the final governance structure is established. Noteworthy, no commitment to a specific contribution to the budget has to be made before the first Work Programme (based on the business plan) and the corresponding budget will be approved by the BBMRI-ERIC Assembly of Members.

The implementation of BBMRI-ERIC comprises the following steps:

- Signature of the Memorandum of Understanding (MoU) that describes the implementation steps and defines which commitments are made at these steps (see Annex V)
- Establishment of a Preparatory Body and of National Nodes to prepare the governing structure of BBMRI-ERIC
- Agreement on the statutes and business plan
- Submission of the BBMRI-ERIC application
- Evaluation of the BBMRI-ERIC application by the European Commission
- Signature of the BBMRI-application by BBMRI-ERIC Members after positive evaluation of the application by the Commission
- Establishment of the BBMRI-ERIC Assembly of Members as described in the Statutes; approval of rules of procedures
- Establishment of subordinate bodies needed for initial operation (Finance Committee and Steering Committee, if needed); drafting of their terms of reference and rules of procedure
- Preparation for the hiring of the Director General (or an interim Director General), decision on initial staff establishment (requires budgetary commitment) and approval of hiring of key personnel for the BBMRI-ERIC Headquarters
- Hiring of the Director General
- Preparation of the first Work Programme (prepared by the Director General and the National Coordinators (BBMRI-ERIC Management Committee) and budget for the approval of the Assembly of Members. This includes initiation of the bidding process for Common Services included in the Work Programme and agreement of the payment schedule of national contributions (BBMRI-ERIC needs a cash flow)
- Approval of the first Work Programme and budget

Fig. 12 - Roadmap towards implementation of BBMRI-ERIC



After formal implementation of BBMRI-ERIC as shown in Fig. 12 there will be the **start-up phase** (2013 – 2015) providing all key infrastructure elements required for operation and providing access to human biological samples and associated data. After establishment of basic operation (1Q2014), interoperability and overall efficacy will be enhanced (2Q2014 – 4Q2015). In order to facilitate access the searchable catalogue of available samples and data will be updated and improved in data quality and granularity for BBMRI-ERIC partner biobanks. Common standards will be implemented and a quality management system established including performance indicators. The focus in the start-up phase will be on human biobanks.
Milestones:
M SU1: Web-portal established 3Q2013
M SU2: Agreements with BBMRI-ERIC Partner biobanks 4Q2013
M SU3: Master templates for CDA, MTA available 4Q2013
M SU4: Updated searchable catalogue for BBMRI-ERIC partner biobanks 1Q2014
M SU5: Common SOPs released 2Q2014
M SU6: Quality of partner biobanks evaluated 4Q2014
M SU7: Performance indicator report 1Q2015
M SU8: Three additional members joined BBMRI-ERIC 4Q2015
M SU9: Acquisition of additional not-Member State funding 4Q2015

The start-up phase will be followed by the **full implementation phase** in 2016. Full implementation is characterized by capacity building as well as extending the operation and functionality of BBMRI-ERIC. This will comprise improved data management capacities and services including the establishment of web-based applications to improve searches on available samples and data thereby increasing speed and efficacy for access. Research services will be implemented. The international master programme for biobank manager will be implemented. Packages to establish or upgrade biobanks in countries with less developed biobanking communities will be provided. These packages comprise a complete description of requirements and procedures to set-up biobanks, biobanking technologies, and open-source data management solutions. The focus of work will be extended from human biobanks to biomolecular resources. Furthermore, the global integration and positioning of BBMRI-ERIC will become a strategic priority.

12. Funding and financing

12.1 General costs of biobanks

BBMRI preparatory phase conducted a survey of the costs and funding of European biobanks. The analysis of 84 biobanks showed that the average cost of running a biobank is of 530 K€ per year excluding the cost of research projects. The distribution of cost between different items is shown in Fig. 13; 41% of this cost reflects salaries related to human resources. While future investment and sample handling represent respectively 19 and 18%.

Fig. 13 - Average cost distribution for operation of a biobank

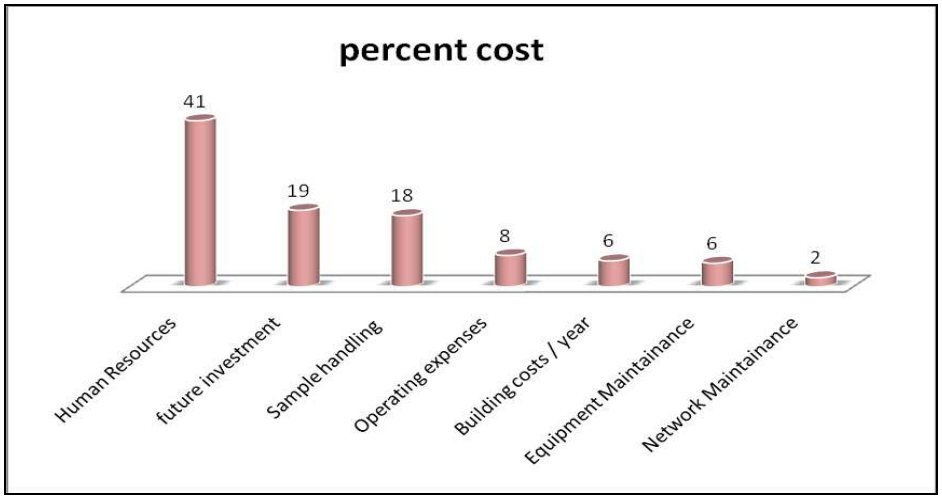
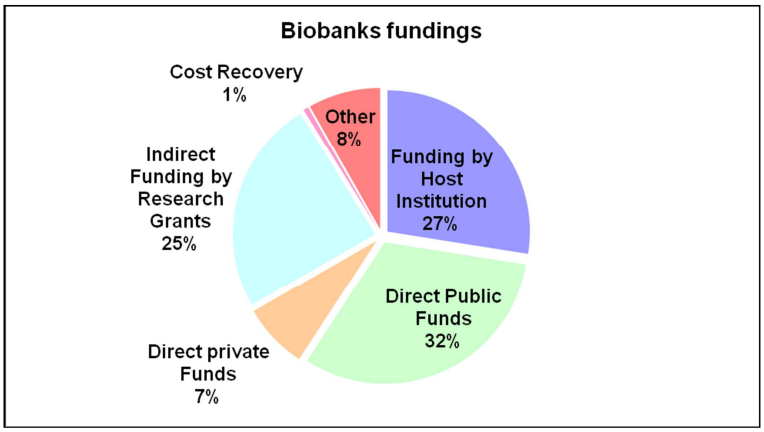


Fig. 14 - Average funding sources for the operation of a biobank



National Networks of Biobanks

BBMRI preparatory phase has already elicited the structuring of biobanks at national levels in several European countries. Thus several countries organized their biobanks in coordinated networks or infrastructures for future participation in BBMRI-ERIC with significant funding of about 135 millions € (Fig. 14).

Table 14 - Funding of national biobanks for future participation in BBMRI-ERIC

State	Biobanks funding € million
Austria	14
Finland	14
France	17
Germany	14
Greece	5
Italy	15
Spain	5
Sweden	14
Czech Republic	4.8
The Netherlands	22.5
Norway	10

12.2 Costs for construction and operation of BBMRI-ERIC

The BBMRI-ERIC governance structure will be implemented by end of 2012, and BBMRI-ERIC is expected to becomes fully operational in the second half of year 2013 (Fig. 12). The cost calculation is based on the assumption that the network will start with ten Member Countries. In the following years two new members will join BBMRI-ERIC each year, so that in 2017 the network will comprise 18 members (Table 18).

Table 15 - Growth of BBMRI-ERIC

Planning Period	2013	2014	2015	2016	2017
Number of Members	10	12	14	16	18

According to the implementation plan (Fig. 12) the Central Executive Management Office as well as the Common Services, which include the Common Information Technology Services, the ELSI Platform and the Stakeholder Forum will be established after approval of the first Work Programme by March 2013. The Common Biobanking and Resources Services will be implemented after the start-up phase in 2016.

This governance structure will be funded together by all Member Countries (Table 16). Detailed financial plans for each of the BBMRI-ERIC entities are summarized in the annex (Annex VI).

Table 16 - Common BBMRI-ERIC budget (k€) with expected growth rate

Planning Period	2013*	2014	2015	2016	2017	2013 - 2017	
	start-up phase			full implementation			
EXPENDITURES							
Central EM Office	776	1.068	1.110	1.529	1.630	**6.113**	*56%*
IT node	239	407	416	659	657	**2.379**	*22%*
ELSI Platform	119	201	205	291	306	**1.122**	*10%*
Stakeholder Forum	81	145	148	161	162	**697**	*6%*
Common Biobanking and Resources Services	0	0	0	303	294	**596**	*6%*
Total Expenditures	**1.215**	**1.822**	**1.879**	**2.943**	**3.049**	**10.908**	***100%***
INCOME							
Member States	946	1.652	1.702	1.833	1.932	**8.065**	*74%*
Research Grants (30%)	0	0	0	883	915	**1.798**	*16%*
Hosting Countries	248	134	135	179	148	**844**	*8%*
Access Fees	21	36	42	48	54	**201**	*2%*
Total Income	**1.215**	**1.822**	**1.879**	**2.943**	**3.049**	**10.908**	***100%***
COSTS PER MEMBER							
Number of Members	10	12	14	16	18		
Average Costs per Member	**98**	**143**	**125**	**117**	**110**		

*: The budget for 2013 is based on the assumption that recruitment of personnel starts in mid 2013.

The common BBMRI-ERIC budget will relate to an annual Work Programme and has to be approved every year by the Assembly of Members. In addition, countries hosting Common Services contribute to the common BBMRI-ERIC budget and access fees generate income. After the start-up phase it is

expected that the additional costs for full implementation will be financed through research grants within the Eighth framework programme, and does not require an increase of Member contributions.

The Common Services will operate only half of the first year, so that their budgets are lower in 2013. As the number of Member Countries increases the total costs of operation will increase from 1.2 million € to 3 million € per year but at the same time the contribution per individual Member will become less.

After the start-up phase the average contribution will be 120.000 € when BBMRI is fully implemented in 2016 and will decrease thereafter due to the increasing number of Member Countries contributing to the common BBMRI-ERIC budget. Economies of scale are responsible for the decrease in 2017 which will continue as the BBMRI-ERIC network grows. Austria as the proposed hosting country of the Central Executive Management Office offered to contribute 100.000 .-€ /per year to cover costs for rental, equipment and, in part, personnel. Countries hosting Common Services fund 100% of investments necessary for office set-up and cover the running costs for rent. The resulting individual annual contributions of hosting countries can be seen in Table 18. In 2013 the majority of investments take place. This is especially true for the Common Information Technology Services which start out with an investment of 100.000 € in 2013. Taken together the hosting countries contribute additional 248.000 € to the Common BBMRI-ERIC Budget in 2013 and in the following years on average 140.000 € per year.

In case only 8 countries will contribute to common BBMRI-ERIC budget or the European economic situation is worsening a minimal budget is foreseen that allows basic operation and is based on a prolonged start-up phase with reduced capacity building (Table 17). The Member State contribution can be frozen at this level for several years until more Members join BBMRI-ERIC or the economic situation improves.

Table 17 – Minimal common BBMRI-ERIC budget (k€) with 8 participating countries

EXPENDITURES	**k€**
Central EM Office	810
IT node	239
ELSI Platform	119
Stakeholder Forum	81
Common Biobanking and Resources Services	0
Total Expenditures	**1.249**
INCOME	
Member States	1.113
Research Grants	0
Hosting Countries	124
Access Fees	12
Total Income	**1.249**

BBMRI-ERIC Membership contribution model

The total costs of BBMRI-ERIC will be financed by cash and in kind contributions of Members and other income. Contributions of Members will be calculated according to the following model:

1) The membership contribution of each Member shall be composed of a base contribution and a variable share. Concerning the base contribution Members are stratified in two groups according to their number of inhabitants:
   1) 20.000 € base contribution for Members whose number of inhabitants is below 3 Million
   2) 25.000 € base contribution for Members whose number of inhabitants equals or exceeds 3 Million
   The overall amount of the variable share proportion is determined by subtracting the overall amount of base contributions from the overall amount of contributions by Members. The overall amount of the variable share is split among Members based on their percentage of total GDP of all Members.

International organizations shall pay 0.1 per mill of their annual regular budget as variable share proportion if they are Members.

The fixed contribution for Observers shall be 30% of the respective category.

None of the Members shall pay more than 25% of the overall amount of contributions by Members/Observers.

Table 18 – Example of Membership contributions to a common BBMRI-ERIC budget of 1.8 mio €

Member	av. GDP [mio €]	% GDP total	base contribution	variable share of residual costs acc. to % GDP	total MS contribution	share of total budget (%)
Austria	282.249	3,07	25.000 €	44.174	**69.174 €**	3,84
Bulgaria	35.452	0,39	25.000 €	5.548	**30.548 €**	1,70
Czech Republic	146.330	1,59	25.000 €	22.902	**47.902 €**	2,66
Estonia	14.414	0,16	20.000 €	2.256	**22.256 €**	1,24
Finland	179.345	1,95	25.000 €	28.069	**53.069 €**	2,95
France	1.955.773	21,26	25.000 €	306.091	**331.091 €**	18,39
Germany	2.493.347	27,10	25.000 €	390.225	**415.225 €**	23,07
Greece	229.816	2,50	25.000 €	35.968	**60.968 €**	3,39
Italy	1.553.363	16,88	25.000 €	243.112	**268.112 €**	14,90
Latvia	18.297	0,20	20.000 €	2.864	**22.864 €**	1,27
Malta	6.020	0,07	20.000 €	942	**20.942 €**	1,16
Netherlands	587.132	6,38	25.000 €	91.890	**116.890 €**	6,49
Norway	304.102	3,31	25.000 €	47.594	**72.594 €**	4,03
Spain	1.058.216	11,50	25.000 €	165.618	**190.618 €**	10,59
Sweden	337.035	3,66	25.000 €	52.748	**77.748 €**	4,32
total	**9.200.891**	**100,00**	**360.000 €**	**1.440.000**	**1.800.000 €**	**100,00**

12.3 National contributions to BBMRI-ERIC

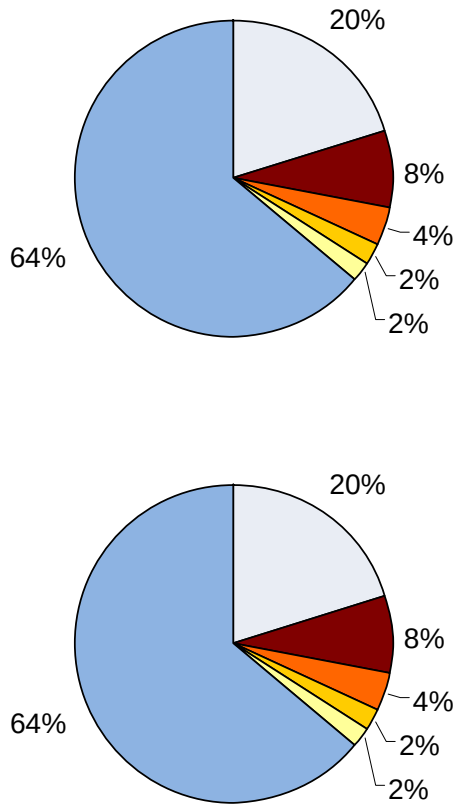
The Members of BBMRI-ERIC will set up their National Nodes under BBMRI-ERIC early in the first quarter of 2013 so that efficient interfaces between national biobanks and the Central Executive Management Office and the BBMRI Common Services can be implemented. The National Nodes are funded directly by each Member Country and are not part of the common BBMRI-ERIC budget. The size of the National Nodes and their budgets will depend on the complexity of the biobanking structures in the individual countries. There are minimal requirements defined for the set-up of a National Node to participate in BBMRI-ERIC. At least one person (National Node Director) reporting to the Director General has to be designated for each National Node. For financial planning National Nodes of an average size are assumed (Table 19).

Table 19 - BBMRI-ERIC budget and national budget of National Nodes

Planning Period	2013	2014	2015	2016	2017	2013 - 2017	
National budgets	**2.651**	**3.208**	**3.817**	**4.450**	**5.106**	**19.231**	***64%***
National Nodes	2.651	3.208	3.817	4.450	5.106	19.231	*64%*
Common BBMRI-ERIC budget	**1.215**	**1.822**	**1.879**	**2.943**	**3.049**	**10.908**	***36%***
Central EM Office	776	1.068	1.110	1.529	1.630	**6.113**	*20%*
IT node	239	407	416	659	657	**2.379**	*8%*
ELSI Platform	119	201	205	291	306	**1.122**	*4%*
Stakeholder Forum	81	145	148	161	162	**697**	*2%*
Common Biobanking and Resources Services	0	0	0	303	294	**596**	*2%*
BBMRI-ERIC budget and National Nodes	**3.866**	**5.030**	**5.696**	**7.393**	**8.155**	**30.139**	*100%*

The cost breakdown of total costs shows that on average 64% of the total costs can be assigned to national budgets funding the National Nodes (Table 19, Fig. 15). BBMRI-ERIC budget required to operate commonly used infrastructure like the Central Executive Management Office (20%) and Common Services (16%).

Fig. 15 - Cost breakdown of total costs for BBMRI-ERIC and National Nodes



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14. Annexes

Annex I: BBMRI Preparatory Phase

BBMRI Participants and Associated Organisations

35 Participants - Scientific Partners

- Medical University of Graz, Austria
- National Institute for Health and Welfare, Finland
- National Research Center for Environment and Health, Germany
- Uppsala Universitet, Sweden
- Karolinska Institutet, Sweden
- University of Manchester, United Kingdom
- International Agency for Research on Cancer, France
- Academisch Ziekenhuis Leiden, The Netherlands
- Norwegian Institute of Public Health, Norway
- University of Malta, Malta
- Norwegian University of Science and Technology, Norway
- Semmelweis University, Hungary
- EGP of the University of Tartu, Estonia
- National DNA Bank, University of Salamanca, Spain
- Helmholtz Gemeinschaft, Germany
- VITRO Ltd, Spain
- Ensembl Functional Genomics, European Genotype Archive, United Kingdom
- Erasmus MC Rotterdam, The Netherlands

19 Participants - Funding Organisations (ministries, research councils)

- INSERM, France
- Fondazione Telethon, Italy
- Féderation hospitalière de France – FHF, France
- Irish Clinical Research Infrastructure Network, Ireland
- Institut National du Cancer, France
- Comitato Nazionale per la Biosicurezza, le Biotecnologie e le Scienze della Vita, Istituto Superiore di Sanita, Italy
- Max-Planck-Institut für Molekulare Genetik, Germany
- Instituto de Salud Carlos III, Spain
- Research Infrastructure and Special Initiatives Unit Health Research Board, Ireland
- Medical Research Council, United Kingdom
- Ministry of Education, Culture and Science, The Netherlands
- The Icelandic Centre for Research, Iceland
- The Netherlands Organisation for Health Research and Development, The Netherlands
- Fraunhofer IBMT, Germany
- Bundesministerium für Bildung und Forschung, Germany
- Bundesministerium für Wissenschaft und Forschung, Austria
- Alleanza Contro il Cancro, Italy

220 Associated Organisations

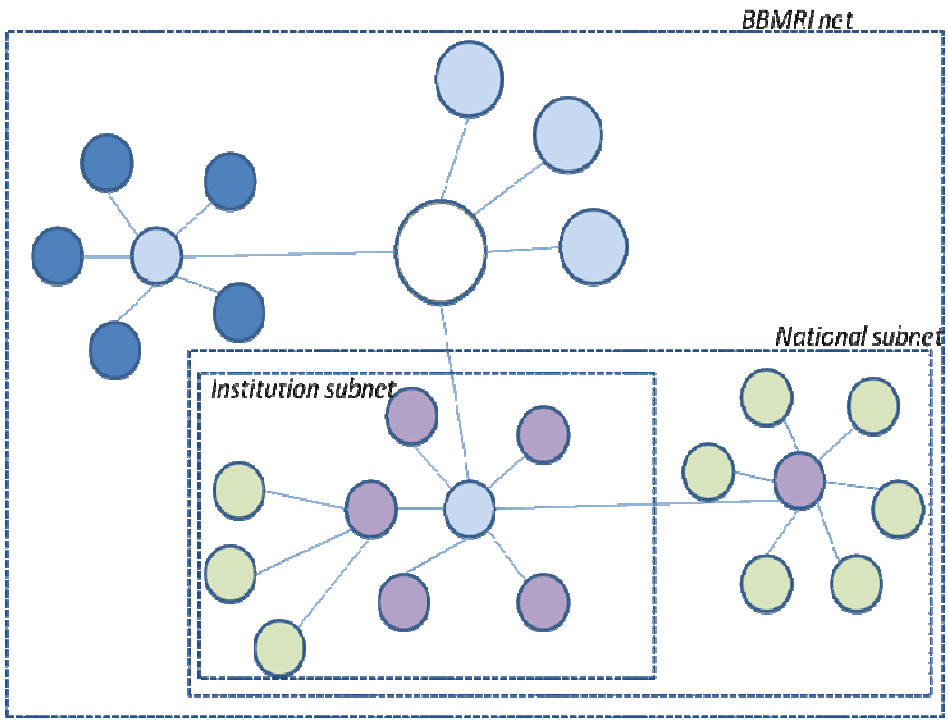
Australia	1
Austria	7
Belgium	10
Bulgaria	1
Canada	2
Cyprus	1
Czech Rep.	1
Faroe Islands	1
Finland	2
France	53
International	1
Germany	31
Greece	1
Hungary	4
Iceland	1
Ireland	2
Israel	4
Italy	22
Luxembourg	1
Malta	1
Martinique	1
Norway	3
Poland	2
Portugal	3
Romania	6
Saudi Arabia	1
Slovenia	1
Spain	14
Sweden	5
Switzerland	3
The Netherlands	23
Turkey	2
UK	9

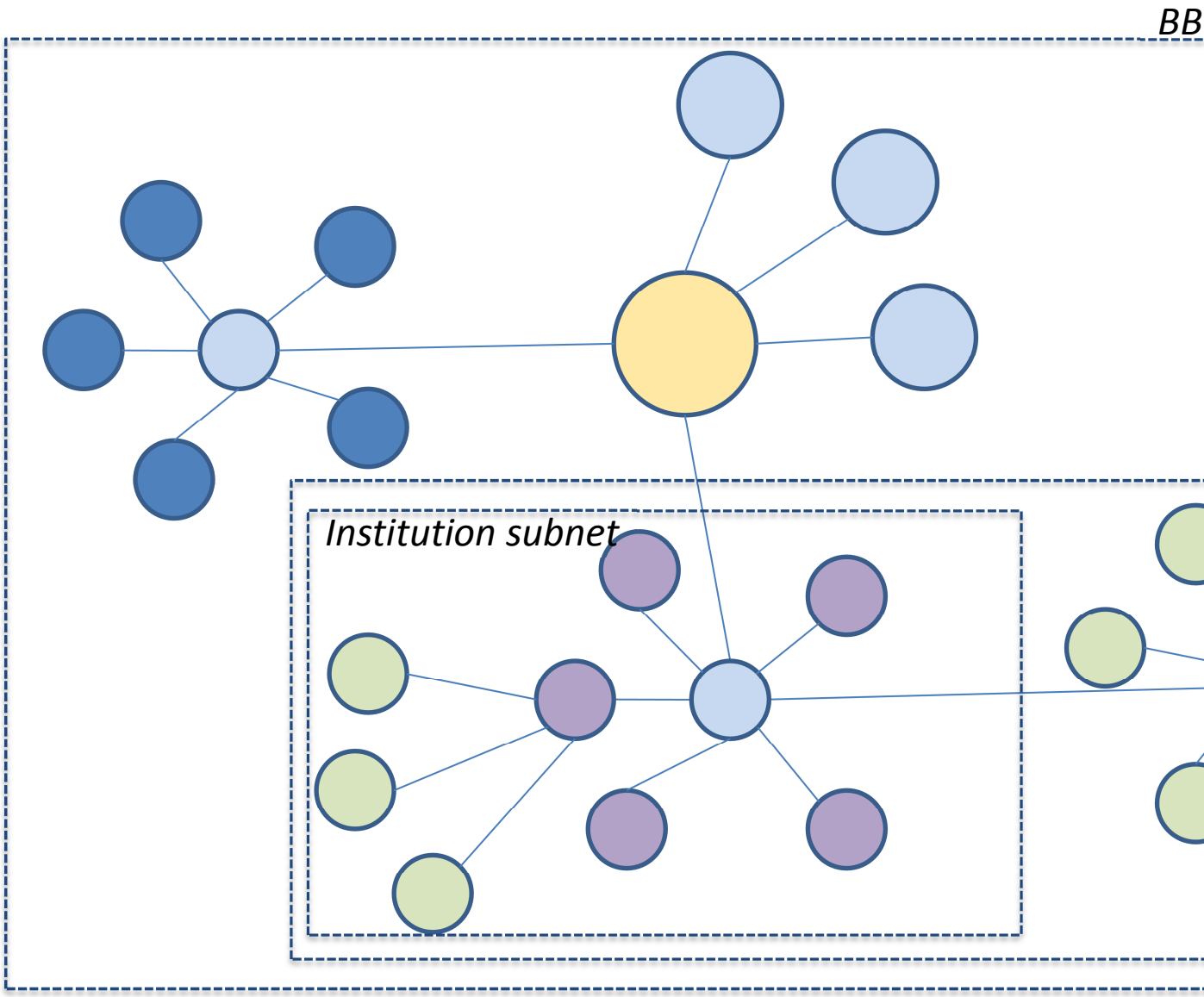
• Istituto Nazionale per la Ricerca sul Cancro, Biological Bank and Cell Factory, Italy • Institute for Biomedical Technologies, Italy • UK Biobank Ltd, United Kingdom • University Hospital Groningen, The Netherlands • Dutch Federation of University Medical Centers, The Netherlands • Legal Pathways b.v., The Netherlands • deCODE genetics, Iceland • Life Science Governance Institute, Austria • Center for Economics and Social Aspects of Genomics, United Kingdom • Babraham Bioscience Technologies, United Kingdom • Hellenic Republic Ministry of Development, General Secretariat For Research & Technology, Greece • Biomedical Research Foundation of the Academy of Athens, Greece • Universitaet Klagenfurt, Austria • University of Turku, Finland • IPPOSI, Ireland • Institut Mérieux, France • IPRI, France	• Fundación para el desarrollo de la investigación en Genómica y Proteómica, Spain • Ministry of Education and Research, Estonia	

BBMRI Preparatory Phase work package leaders and chairs	
Coordination & Management – WP 1	Kurt Zatloukal (coordinator), AT Martin Yuille (deputy-coordinator), UK Eero Vuorio (executive manager), FI Markus Pasterk, (global interactions), FR
Population-based Biobanks – WP 2	Leena Peltonen†, FI Markus Perola, FI Andres Metspalu, EE
Clinical-oriented Biobanks – WP 3	Erich Wichmann, DE Thomas Meitinger, DE
Biomolecular Resources – WP 4	Ulf Landegren, SE Mike Taussig, UK
Databases & Biocomputing - WP 5	Jan-Eric Litton, SE
Ethical, Legal and Societal Issues - WP 6	Anne Cambon-Thomsen, FR
Funding and Financing – WP 7	Georges Dagher, FR Jeannette Ridder, NL Christian Bréchot, FR
Governance Council Chair	Gert-Jan van Ommen, NL Leena Peltonen†, FI/Eero Vuorio, FI
Scientific and Ethical Advisory Board Chair	Gert-Jan van Ommen, NL
Steering Committee	Leena Peltonen†, FI/Eero Vuorio, FI
Coordination Board Chair	Kurt Zatloukal, AT
Stakeholder Forum Chair	Michael Griffith, IR

Annex II: Technical description of Common Information Technology Services

Key components of BBMRI-ERIC are comprehensive collections of biological samples from different (sub-) populations in Europe, which are being stored together with continuously updated data on the health status, lifestyle and environmental exposure of the sample donors, resulting in a significant number of repositories with annotated biospecimens distributed across Europe. BBMRI's goal is to interlink these valuable resources across Europe in order to foster co-operation and research on a pan-European level. Ethical, legal, and societal implications have to be considered carefully in this process, which has to comply with the European Directive on Protection of Personal Data (Directive 95/46/EC). The optimal solution will be a federated network of centres established in most, if not all, European Member States (Muilu et al., 2007), and the topology of BBMRI-ERIC will be a distributed hub structure in which the hubs coordinate activities, including collection, exchange and analysis of samples and data for the major domains.


BBMRI net
National subnet
Institution subnet



The distributed hub and spoke structure of BBMRI-ERIC. Biobanks, biomolecular resources and technology centres are partners of BBMRI-ERIC and connected to their specific hub.

BBMRI PP has created the necessary IT-concepts, architectural components, and prototypical solutions for an adequate and effective support of this network. The solution will be a light-weight, virtual integration approach based on federated databases. It will connect the complex network of hubs, members and partners into a single virtual structure, preserving privacy and autonomy on one hand, and supporting communication and collaboration on the other hand.
Use cases and key requirements have been collected and are available as a result of BBMRI PP. Furthermore, minimal data sets, service concepts and the schema architecture have been defined. The federated database system will enable searching for interesting and comparable material across European biobanks. Special emphasis has been given to confidentiality, privacy and the adherence to special procedures for disclosure put in place by the participating biobanks.
Considering the multilingualism of Europe, an online multilingual biobank terminology system and management environment will be developed using the ConceptWiki approach. This is a major step towards true end-user interoperability, for the first time systematically lowering the language barrier between descriptions of cross-European biobanks.

Based on the results of BBMRI-PP, the IT structure for ERIC can be developed; it will

- Assure confidentiality of donors
- Use state-of-the art open-source frameworks and web technologies

- Use state-of-the art concepts for semantic integration, integrating the terminologies/ ontologies to be further developed by the ConceptWiki project
- Use an agile and user-centred development process, providing maximum support for researchers
- Grant flexibility in terms of biobank content and schema handling
- Grant extensibility in terms of additional participants and new data and information
- Grant efficiency in terms of a priori and a posteriori data harmonization and query processing
- Keep efforts low for biobanks willing to participate in the federation

We will collaborate closely with other biobanking/health infrastructure initiatives (such as IMI, epSOS and HEALTH.2010.1.1-1: Harmonisation of phenotyping and biosampling for human large-scale research biobanks), Gen2Phen EU- project and the DataShaper project to reach interoperability of biobanks, both at the concept- and at the sample character (comparability) level.
The most significant outcome of the BBMRI-PP WP5 has been the development and deployment of a portal system and the development of an integration prototype. The portal system already comprises services for authentication and management of user accounts for identification of biobanks, and for the management of metadata. The integration prototype is already connected to test-instances of existing biobank management systems and provides a service interface for the creation, update and querying of a materialized view. These developments can be used as a nucleus for a service-oriented integration architecture, which is supporting high adaptability and agile development of components. Core services have been designed and implemented and can be further elaborated into a comprehensive integration architecture. Additional services will comprise connection and registration services for the component systems, services for schema integration and terminology mapping, integration services for virtual and secure access of component systems in order to build and query materialized views with regard to semantic integration, as well as services for caching and indexing. The topology of the solution is hub and spokes. Hubs collect and integrate data, but can also provide a data connection service. This results in cascading hubs and spokes, connecting biobanks to regional networks, further to national hubs, and finally to a pan-European BBMRI hub. Thus, key requirements and key concepts together with a successful prototypical solution are available as a starting point for implementing ERIC's IT infrastructure. Figure 2 shows an architectural overview.
Today, sample collections are typically described with metadata captured in the commonly used language of the countries in which they are collected, especially when the sample collection or textual information is linked to electronic medical record systems or other health care related data structures. The 'tags' that are currently used in metadata fields are mostly either free text key words or at best identifiers from controlled (locally developed) vocabularies or ontologies.
To improve interoperability, a well-mapped and open terminology system will be realized. Development work will include translations (by national communities) of all biomedical relevant terms into all community languages, and expansion of the Concept Wiki. Collaborating groups can add terminology systems batch-wise, with the in-built possibility to review and authorize such additions by recognized experts. The existing minimum data set is ready to be extended in a domain-specific manner (e.g., for cancer biobanks). The Concept Wiki will serve as the reference in this process.

Need of resources
The following positions (Full-Time Employment) have been estimated(*) to be required for the BBMRI IT-node in an ERIC:

- 1 Project manager – will lead the Informatics team of the IT-node, plus external contractors, and hold overall responsibility for developing and supporting standards, user interfaces/data portal, the Concept Wiki and the physical IT-infrastructure.
- 1 Systems architect – responsible for concepts, and for the database and application architecture
- 1 Software developer, responsible for the Concept Wiki, terminologies, and standards
- 1 Software developer, responsible for the databases and the middleware
- 1 Software developer, responsible for application development, user interfaces, and process support
- 1 Maintenance programmer– responsible for user feedback and user support
- 1/2 associate project manager

The BBMRI-IT node will be established after an open call procedure among BBMRI-ERIC Members. A prototypical solution have been launched during the preparatory phase in Sweden, Munich and Klagenfurt/Graz that can be used as parts of BBMRI-ERIC's final IT infrastructure.

- Estimation of required resources has been performed by looking at the composition of the Global Biodiversity Information Facility (GBIF) secretariat staff. The secretariat consists of 24 positions of which of at 11 positions are estimated to relate directly to IT and informatics.

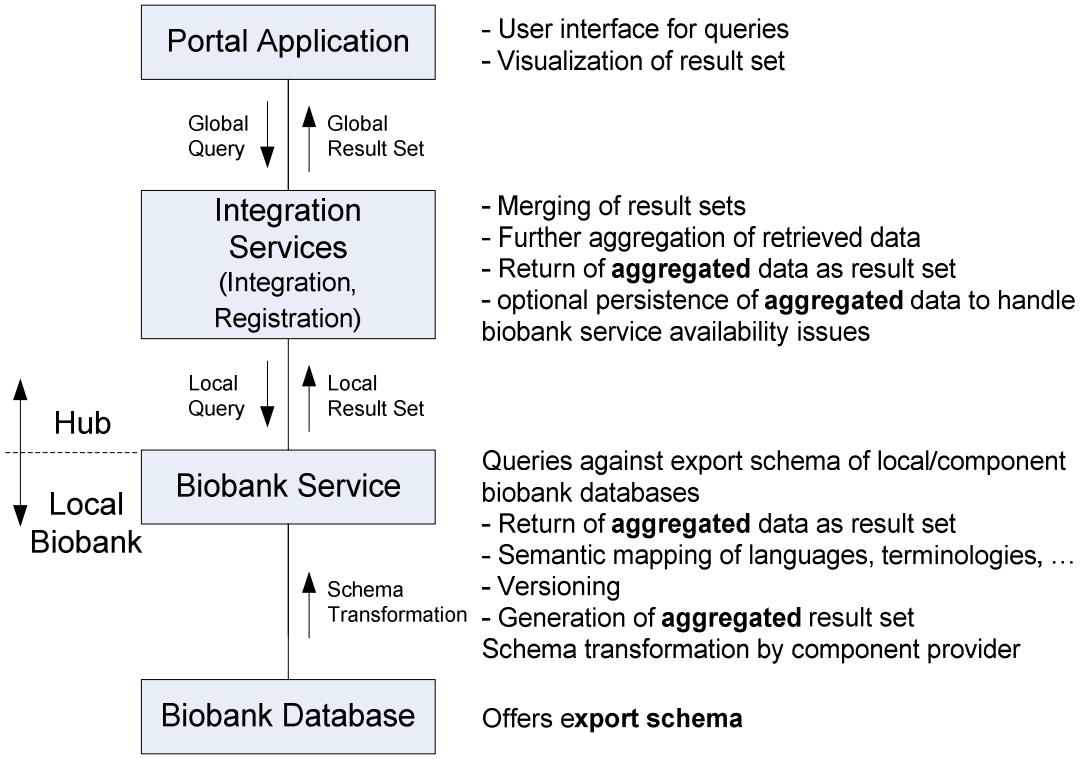
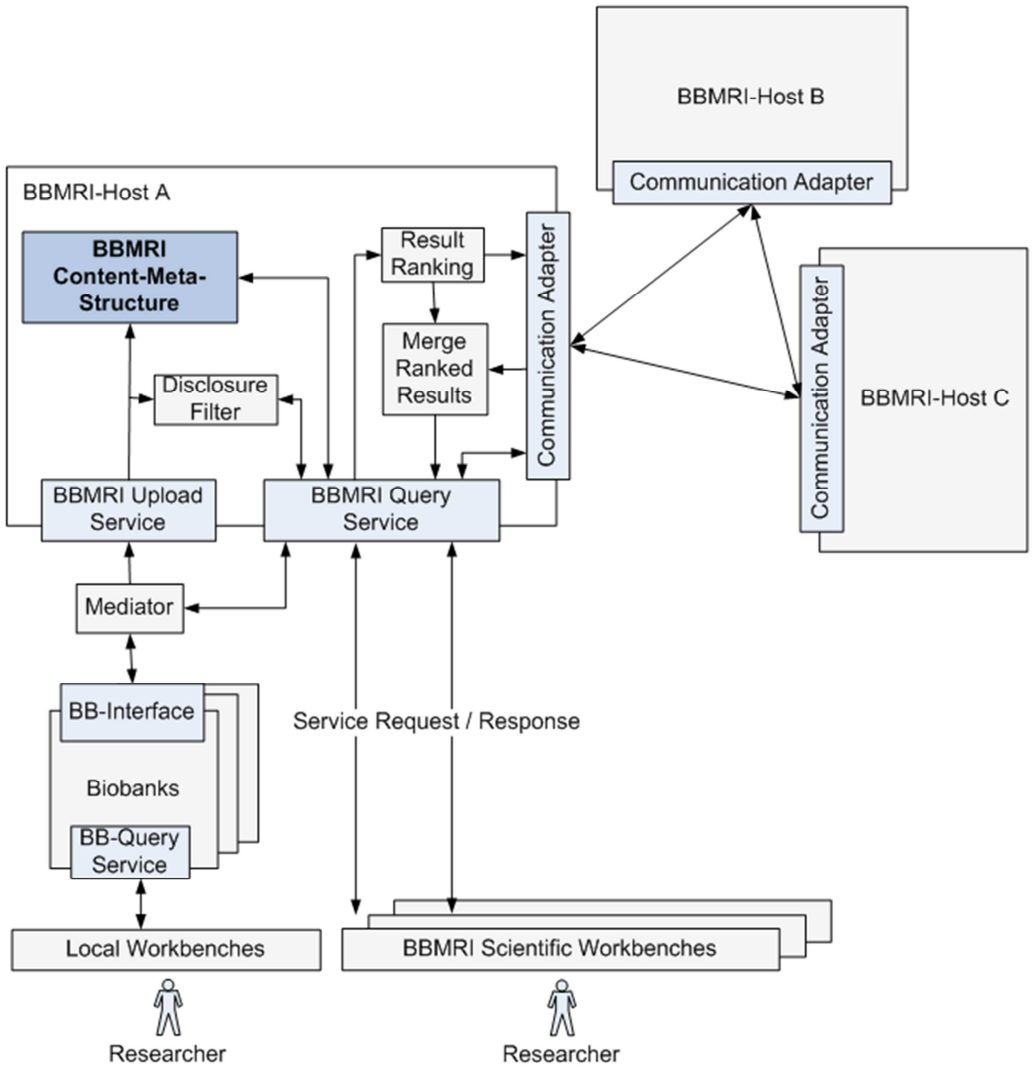


Figure 2. Services connecting biobanks and hubs


BBMRI-Host B
Communication Adapter
BBMRI-Host A
BBMRI Content-Meta-Structure
Result Ranking
Merge Ranked Results
Communication Adapter
Disclosure Filter
Communication Adapter
BBMRI-Host C
BBMRI Upload Service
BBMRI Query Service
Mediator
BB-Interface
Biobanks
BB-Query Service
Service Request / Response
Local Workbenches
BBMRI Scientific Workbenches
Researcher
Researcher

Minimum data set

Data describing biobanks		
Definition	**Allowed values**	**Explanation**
BiobankAcronym	ASCII	
NameOfBiobank	Free text in English	
Institution	Free text in English	
URL		
Country	ISO-standard (3166 alpha2), two letter code	
ContactName	Free text in English	
ContactData	Free text in English	Address, Phone (E.164, No. 905 – 1.IV.2008), e.g., +46 8 524 877 59, Mail
Data describing studies		
Definition	**Allowed values**	**Explanation**
NameOfStudy	Free text in any language	
EnglishStudyName	Free text in English	Translantion of study name in English
ContactName	Free text in English	
ContactData	Free text in English	Address, Phone (E.164, No. 905 – 1.IV.2008), e.g., +46 8 524 877 59, Mail
KindOfStudy	Population-based, specific-disease, broad-spectrum of diseases	If "specific-disease", note ICD10
CategoriesOfDataCollected	[ClinicalDataAvailable, Diagnosis, Health information, Physiological/biochmical measures, Sociodemographic char., Socioeconomic char., Life habits/Behav., Physical environment]	Can be several values
Data describing subjects/cases/samples within biobanks		
Definition	**Allowed values**	**Explanation**
AgeGroup	Interval [a,b], a>0, b<200, b>=a	a and b should be selected so that k-anonymity is guaranteed. Age group of donor at time for sample collection, number of age groups determined by biobank
Gender	Male, Female, Other	Gender of subject
SampleType	DNA, cDNA/RNA, whole blood, blood cells isolates, serum, plasma, fluids, tissues cryo, tissues paraffin-inbedded, cell-lines	Type of sample. From the BBMRI core question.
SampleDate	ISO-standard (8601) time format	Date when sample was harvested
ClinicalDataAvailable	Yes/No	There exists clinical data related to the sample
OrganCategory	From the BBMRI Detailed descr bio samples	
OmicsDataAvailable	Yes/No	Genomics, proteomics etc
RestrictionsOnSampleUse	None, Consent participant, IRB approval, Approval of owner of collection	Can be several values

NOTES:

Time stamp and version control are part of the meta-data schema and upload services

Annex III: Partner Charter

The European Research Infrastructure for Bio-Banking and Biomolecular Resources

Partner Charter

(Draft version 5; 18.6.2012)

Purpose and applicability

The BBMRI-ERIC Partner Charter should define the most important cornerstones for the participation of biobanks or biological resource centres (Partner) that are associated with BBMRI-ERIC to foster scientific excellence, guarantee interoperability, and compliance with ethical and legal requirements. The Partner Charter is binding for any Partner of the BBMRI-ERIC and shall be agreed between national BBMRI-ERIC nodes and the Partners. Participation of a Partner in BBMRI-ERIC is non-exclusive and has no effect on any activity of a Partner outside of BBMRI-ERIC.

Principles

Primacy

BBMRI-ERIC acknowledges the primacy of national and European legislation and respects the jurisdiction of competent authorities.

Access policy

Samples and data need to be accessible through a clear access procedure compliant with the general access procedures and conditions of BBMRI-ERIC. BBMRI-ERIC will foster the establishment of scientific collaborations between authenticated scientific users and Partners. Special access policies can be established for industrial users.

Access to samples and data will honour commitments to donors and follow the principles of “fair access” and scientific excellence. Access in the context of research projects performed within BBMRI-ERIC will only be provided for specified research projects, in accordance with the terms of the consent given by the participant and after approval of the research project by a Research Ethics Committee (REC). Access has to be compliant with regulations of BBMRI-ERIC Partner biobanks, and Partner biobanks have to decide whether access can be granted for a specific project. This decision has to follow transparent and non-discriminating decision making procedures. Noteworthy, the establishment of high quality research collaboration is the preferred format for access.

Data protection and management policy

BBMRI-ERIC and Partners will not make public any information of research projects performed through BBMRI-ERIC that can be directly related to an individual. Information on individuals will only be made accessible to authenticated scientific users in a coded or anonymized fashion in the context of specific research projects and upon approval by a competent Research Ethics Committee (REC) in compliance with national and EU legislation, and subject to the BBMRI data access conditions. Partners will support integration of their data management system with that of BBMRI-ERIC by complying with the BBMRI-ERIC information requirements. The initial information requirements are realised as the expected minimal common data content and data structure in relevant databases. No access will be provided for non-research purposes (such as forensic, insurance or employment purposes), except pursuant to a court order.

Informed consent

BBMRI-ERIC and Partners will, at any time, honour commitments owed to donors. Partners shall aim at prospectively implementing the OECD Guidelines for Human Biobanks and Genetic Research

Databases for issues related to informed consent, as appropriate and subject to the primacy of national and EU legislation.

Infrastructure and management

Partners will commit themselves to future implementation of the OECD best practice guidelines for Global Biological Resource Centres Networks. These guidelines define in particular requirements concerning the following issues:

- Infrastructure (building, facility)
- Management (responsibilities and qualifications)
- Traceability
- Biosecurity
- Data protection
- Minimal and recommended datasets
- Quality management and certification

Quality management

All Partners should commit themselves to implement quality management /assurance procedures compliant with OECD best practice guidelines for Global Biological Resource Centres Networks. SOPs should be established and made publicly available for all processes related to sample collection, processing, storage, retrieval and despatch. It is recommended that SOPs should follow the procedures as specified in the WHO/IARC guidelines for biological resource centres for cancer research whenever feasible. A unique BBMRI biobank (collection) identifier should be provided (see Kauffman, F & Cambon-Thomsen, A). Tracing biological collections: Between books and clinical trials. JAMA 2008, 299: 2316-2318). Criteria for the identifier will be provided by BBMRI-ERIC. Partners should allow external audits by BBMRI-ERIC.

Reporting

Partners will provide annual reports to the National Node Director on which research projects have been supported and information on the outcome that partners have received (e.g., publications, patents). Projects that have been supported by BBMRI-ERIC should acknowledge the contribution of BBMRI-ERIC in any publication according to the principles of good scientific practice. Partners will provide a yearly updated inventory to the National Node Director on the type, content and quality of collections and resources they are holding.

Charges

BBMRI-ERIC will pursue its principal task on a non-economic basis. However, it may carry out limited economic activities, provided that they are closely related to its principal task and that they do not jeopardise the achievement thereof. Biobanking-related services might be subject to cost recovery. Costs can be recovered for staffing, consumables, licensing, equipment servicing/maintenance. No patient samples or data are sold for profit. Supply of samples by or to external commercial organisations shall be conducted in accordance with the Community Framework for State Aid for Research and Development and Innovation (2006/C 323/01).

Annex IV: Examples of Relevant EU Legislation and International Conventions and Regulations

Relevant EU legislation such as:

- The Charter of Fundamental Rights of the EU
- Directive 95/46/EC of 24 October 1995 on the protection of individuals with regards to processing of personal data and the movement of such data
- Directive 2001/20/EC of 4 April 2001 on clinical good practice
- Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.
- Directive 2004/33/EC as regards information to be provided to prospective donors, information required from donors, eligibility of donors; storage, transport and distribution conditions for blood and blood components; quality and safety requirements for blood and blood components
- Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions
- Directive 86/609/EEC of 24 Nov. 1986 on the protection of animals
- Directive 86/609/EEC of 24 Nov. 1986 on the protection of animals used for experimental and other scientific purposes
- Protocol on Protection and welfare of animals (protocol to the Amsterdam Treaty)
- Directive 2000/54/EC of the European Parliament and of the Council of 18 September 2000 on the protection of workers from the risks related to exposure to biological agents at work (7th individual directive within the meaning of Article 16(1) of Directive 89/391/EC)
- Directive 2004/23/EC of the European Parliament and of the Council on Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells", code number 2002/0128 (COD), Strasbourg, 31 March 2004.
- Directive 2002/98/EC setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components.
- Directive 98/44/EC on the legal protection of biotechnological inventions.

International conventions, declarations, and guidelines:

- Helsinki Declaration in its latest version
- Convention of the Council of Europe on Human Rights and Biomedicine signed in Oviedo on April 4, 1997, and the Additional Protocol on the Prohibition of Cloning Human Beings signed in Paris on 12 January 1998
- Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological material of human origin
- UN Convention on the Rights of the Child
- Universal Declaration on the human genome and human rights adopted by UNESCO
- OECD Best Practice Guidelines for Biological Resource Centres, OECD 2007
- OECD Guidelines on Human Biobanks and Genetic Research Databases. OECD 2009

Annex V: Memorandum of Understanding

Memorandum of Understanding

For the establishment of
The Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium (BBMRI-ERIC)

THE SIGNATORIES, CONSIDERING:

- In 2004, the European Strategy Forum on Research Infrastructures (ESFRI) was given the mandate from the Council of the European Union to develop a European Strategic Roadmap for Research Infrastructure. The aims were to describe the scientific infrastructural needs for the next 10 to 20 years. In 2006 ESFRI published its report, the “European Roadmap for Research Infrastructure”, followed by a first update in 2008. The ESFRI Roadmap identifies infrastructures in all fields which are vital for research and which should be realised on a European level.

- The Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) was among the first six ESFRI initiatives in the field of biological and medical sciences for which an implementation was recommended. It therefore received 'Preparatory Phase' funding from the European Commission through the “Capacities” Programme of the Seventh Framework Programme.

- The aim of BBMRI is to establish, operate and develop a pan-European distributed research infrastructure of population-based and disease-oriented biobanks and biomolecular resources in order to provide resources, facilities and support to high quality biological and medical research at all stages of the biomedical R&D process. BBMRI will grant for the European researchers effective access to its resources and Common Services that include a joint IT service, and provision of scientific, technical, ethical and legal expertise.

- The Preparatory Phase of BBMRI is funded by the European Commission for the years 2008-2010. This Preparatory Phase aims to define a viable concept for a research infrastructure on biobanking and biomolecular resources, including the setting up of a legal framework, access conditions and a sustainable financial plan to operate it. The participants of the Preparatory Phase have been both scientific institutions (“Scientific Partners”) and “Governmental Partners”.

- The Governmental Signatories, along with the Scientific Partners, envisage to adopt the European Research Infrastructure Consortium (hereinafter “ERIC”) set up by Council Regulation (EC) n°723/2009 of 25 June 2009 as the legal structure for BBMRI.

- In parallel, the Signatories envisage to enter a process to prepare BBMRI-ERIC. The aim of the process is to prepare BBMRI-ERIC and to start up the delivery of BBMRI services by the participating biobanks and biomolecular resource providers. The BBMRI National Nodes and Common Services will start with pilot projects on a smaller scale, expand progressively and gradually build up capacities and missing components where needed.

THEREFORE AGREE, WITHOUT MAKING A LEGAL COMMITMENT, AS FOLLOWS:

PARAGRAPH 1: PURPOSE AND NATURE OF THIS MEMORANDUM OF UNDERSTANDING

The purpose of this Memorandum of Understanding (hereinafter "the MoU") is to settle the intent of the Signatories regarding the following steps to be taken towards the setting-up of BBMRI-ERIC. To this end, the Signatories may provide each other with all necessary relevant information.

Nothing in the MoU will be deemed to constitute any commitment to become a Member of the BBMRI-ERIC or any other legal entity governing the BBMRI infrastructure.

The MoU is neither a contract nor a treaty, but a declaration of intention and therefore legally not binding.

PARAGRAPH 2: IMPLEMENTATION OF A LEGAL STRUCTURE

The Signatories intend to make their best efforts to diligently follow all the necessary steps required to apply for a European Research Infrastructure Consortium (ERIC) legal entity, as described in Council Regulation (EC) n°723/2009 of 25 June 2009.

The Signatories will not be entitled to act or to make any legally binding declarations or commitments on behalf of any other Signatory unless duly authorised in writing by the concerned Signatory or Signatories.

PARAGRAPH 3: CONTRIBUTIONS

Each Signatory declares its intention to evaluate the possibility:

- to establish BBMRI-ERIC with the statutory seat in Austria,
- to support the establishment of a BBMRI National Node and appoint a coordinator (National Coordinator) for the National Node,
- to establish such preparatory bodies as deemed necessary,
- to integrate its national biobanking institutions and biomolecular repositories that are eligible for the participation in BBMRI-ERIC,
- to seek consensus regarding the principles of determining the mandatory national contributions to the common budget of BBMRI-ERIC to support the BBMRI-ERIC Central Executive Management Office and the BBMRI-ERIC Common Services.

The Signatories agree not to withhold information that is relevant for implementation of the MoU.

PARAGRAPH 4: PREPARATORY STRUCTURE

The process of establishing BBMRIERIC as a legal entity will be governed by a preparatory structure consisting of one representative of each country signatory to the MoU. These representatives are appointed by the Signatories.

An preparatory body consisting of the National Coordinators of countries signatory to the MoU will act upon a mandate given by these representatives.

The Signatories will cover all the costs of the participation of their representatives. The Signatories agree that they will seek to reach consensus and follow the principle of "one vote per signatory" in the decisions made.

Non-signatory countries or intergovernmental organisations that nonetheless have a clear intention of signing the MoU may also be invited to attend meetings as observers but shall not have a vote until they have become co-signatories of the MoU.

PARAGRAPH 5: COMING INTO EFFECT AND DURATION

The MoU shall come into effect between the Signatories that have signed it as of the day on which the third Signatory has signed it. It shall then come into effect regarding each additional Signatory that signs it after this date as of its date of signature by said Signatory.

It shall remain in effect:

- until the BBMRI-ERIC or any other legal form has been established, or
- for a period of twenty-four (24) months as of the day on which the third Signatory has signed

which ever of these dates comes first.

As this MoU is legally not binding, the Signatories may decide to terminate it earlier. In this case, the Signatory deciding the termination will inform the other Signatories in writing subject to a three months prior notification. The remaining Signatories may decide to maintain the MoU in effect among them for the initial duration as specified in the present paragraph or to terminate it.

If the MoU is terminated by one, several or all Signatories, neither Signatory shall be liable to the other Signatory for any monetary or other losses that may result.

PARAGRAPH 6: AMENDMENT AND ASSIGNMENT

Any modification of the MoU requires the written agreement signed by all the Signatories hereto.

No rights or obligations of any of the Signatories arising from the MoU may be assigned or transferred in whole or in part to any third party without the other Signatory's or Signatories´ prior written approval.

PARAGRAPH 7: RESOLUTION OF DISPUTES

Disputes that might arise concerning the MoU will be settled amicably. If no amicable solution is possible, the Signatories will terminate the MoU.

PARAGRAPH 8: COPIES

Done in as many copies as there are Signatories, each of them being equally valid.

Memorandum of Understanding

For the establishment of
The Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium (BBMRI-ERIC)

Signatory full legal name:

Acronym:

Entitled authority (Title, Family name, First name):

Position:

Date:

Signature:

Stamp or seal of the organisation:

Annex VI: Financial Plan – Details

1. Central Executive Management Office

Table 20 - Financial plan for the Central Executive Management Office from 2013 to 2017 (in EURO)

Planning Period	2013	2014	2015	2016	2017	2013 - 2017		Note
	start-up phase			full implementation				
RECEIPTS								
Member States	655.253	932.350	967.798	922.333	986.924	4.464.657	*73%*	(1)
Research Grants (30%)	0	0	0	458.714	488.968	947.682	*16%*	(2)
Hosting Country	100.000	100.000	100.000	100.000	100.000	500.000	*8%*	(3)
Access Fees	21.000	36.000	42.000	48.000	54.000	201.000	*3%*	(4)
Total Financing	**776.253**	**1.068.350**	**1.109.798**	**1.529.047**	**1.629.892**	**6.113.339**	***100%***	
EXPENDITURES								
Personnel Costs	**430.000**	**622.200**	**634.644**	**1.050.596**	**1.136.554**	**3.873.994**	*63%*	(5)
Investments	**47.000**	**4.000**	**20.000**	**15.000**	**10.000**	**96.000**	*1%*	(6)
Other operating expenditures	**299.253**	**442.150**	**455.154**	**463.451**	**483.338**	**2.143.345**	*35%*	
Rent	17.640	27.418	27.966	42.788	47.281			(7)
Consumables	4.250	14.280	14.566	25.469	28.143			(8)
Travel	100.000	106.080	112.363	118.855	125.562			(9)
Assembly of Members	20.000	20.400	20.808	21.224	21.649			(10)
Scientific conference	30.000	30.600	31.212	31.836	32.473			(11)
Office	2.363	3.672	3.745	5.731	6.332			(12)
Education and Training	25.000	25.500	26.010	26.530	27.061			(13)
Outsourcing	100.000	214.200	218.484	191.017	194.838			(14)
Total Expenditures	**776.253**	**1.068.350**	**1.109.798**	**1.529.047**	**1.629.892**	**6.113.339**	*100%*	

The financial plan for the Central Executive Management Office is based on the following assumptions.

- Annual rate of inflation: 2%
- VAT is excluded
- Start of operation: 01/2013 - Employment of Director General
  06/2013 – Employment of basic personnel

(1) Contribution per Member:

Planning Period	2013	2014	2015	2016	2017
Number of Members	10	12	14	16	18
Contribution / Member	44.874	57.414	50.320	63.041	60.772

(2) Research Grants:

- 30% of financing will be covered by EU grants

(3) Hosting country:
Countries hosting Common Services (Central Executive Management Office, IT Services, Stakeholder Forum, ELSI Platform, Biobank Research Services) contribute 100% of the costs for rent and investments.

(**4) Access fees:**

- 1 project / member / year
- Average project fee: 3.000 €
- The project fee includes
    - o a project set-up and processing fee: 2 reviews (scientific, ethical), 150€ / reviewer
    - o contribution to administrative and project management costs: the costs will increase with the complexity of the project (the number of samples and the number of centres involved)
    - o not included are costs for biobanking-related services and samples of biobanks in different Member Countries, these will be defined in each country, respectively

The aim is that after the roll out phase a fair fee shall be charged as an incentive to use the BBMRI-ERIC network and to propose projects with scientific excellence. It is not intended to reach self - sustainability by charging project fees. When the BBMRI-ERIC network will be used in EU or nationally funded research collaboration, part of the costs will be covered by those grants.

(5) Personnel Costs:

Initially it is envisaged that the personnel as shown in Table 7 will be hired for the Central Executive Management Office (see chapter 10.3.1).

Development of Central Executive Management Office personnel from 2013 to 2017:

Function	2013	2014	2015	2016	2017
Director General	1,00	1	1	1	1
Administrative Director	0,75	1	1	1	1
Lawyer	outsourcing			1	1
IT/Data protection	0,25	0.5	0.5	1	1
Quality management	0,25	0.5	0.5	1	1
Project manager	0,50	1	1	2	2
Assistant	0,50	1	1	2	3
Secretary	1,00	2	2	3	3
Total FTEs*	**4,25**	**7**	**7**	**12**	**13**
Number of employees	7	8	8	12	13
* Full time equivalent			**capacity building**		

Function	Annual Salary
Director General	180.000*
Administrative Director	140.000
Lawyer	120.000
IT/Data protection	120.000
Quality management	80.000
Project manager	70.000
Assistant	60.000
Secretary	30.000

Annual salaries including fringe benefits

Starting salaries in 2013, annual inflation rate: 2%

*: In addition to salary success-depended benefits may be negotiated

(6) Investments:

Investments	Period of usage (years)	Costs/Person
Furniture	10	1.000
IT infrastructure*	5	4.000
Electrical	10	3.000
Other appliances	10	2.000

*including desktop/laptop, server, software, network cabling, printer, fax/copier/scanner, mobile phones

(7) Rent:
- Office for 7 employees as of Q2/2013, flexible growth of office size with capacity building
- 3.360 € / person /year, 14 € / sqm /month, on average 20 sqm /person (including electricity, water, gas, meeting rooms)

(8) Consumables:
- 2.000 € / person /year

(9) Travel:
- 1000 € / trip, + 2.000 € for each additional Member Country (see Table 15)

(10) Assembly of Members:
- 2 meetings /year, excluding travel costs

(11) Scientific Conference:
- 1 conference /year

(12) Office:
- Telephone, stationary: 450 € / person /year

(13) Education and Training:

An exchange programme will be implemented, that enhances transnational know-transfer by funding 2-4 month long stays of scientists in other centres. Applications to calls of the programme will be peer reviewed and evaluated by a scientific review board. It is intended to apply for additional funding for 'Education and Training' from other sources.

(14) Outsourcing:
- Marketing, consulting audits: 150.000 € / year
- from 2013 to 2015 legal advice will be sourced out, accounting will be sourced out from 2013 to 2017

Planning Period	2013	2014	2015	2016	2017
Lawyer	30.000	30.600	31.212	lawyer employed	
Accounting	20.000	30.600	31.212	31.836	32.473

2. *Common Information Technology Services*

Table 21 - Financial plan for the Common Information Technology Services from 2013 to 2017 (in EURO)

Planning Period	2013	2014	2015	2016	2017	2013 - 2017		Note
	start-up phase			full implementation				
RECEIPTS								
Member States	130.250	392.190	400.034	427.306	440.442	1.790.221	*75%*	(1)
Research Grants (30%)	0	0	0	197.746	197.111	394.857	*17%*	(2)
Hosting Country	109.000	15.300	15.606	34.102	19.484	193.492	*8%*	(3)
Total Financing	**239.250**	**407.490**	**415.640**	**659.153**	**657.036**	**2.378.569**	*100%*	
EXPENDITURES								
Personnel Costs	**78.750**	**283.050**	**288.711**	**509.380**	**519.567**	**1.679.458**	*70,6%*	(4)
Investments	**100.000**			**15.000**		**115.000**	*4,8%*	(5)
Other operating expenditures	**60.500**	**124.440**	**126.929**	**134.773**	**137.469**	**584.111**	*24,6%*	
Rent	9.000	15.300	15.606	19.102	19.484			(6)
Consumables	3.000	10.200	10.404	12.734	12.989			(7)
Meetings	5.000	10.200	10.404	10.612	10.824			(8)
Travel	18.000	36.720	37.454	38.203	38.968			(9)
Outsourcing	20.000	40.800	41.616	42.448	43.297			(10)
Miscellaneous	5.500	11.220	11.444	11.673	11.907			
Total Costs	**239.250**	**407.490**	**415.640**	**659.153**	**657.036**	**2.378.569**	*100%*	

The financial plan for the Common Information Technology Services is based on the following assumptions.

- Annual rate of inflation: 2%
- VAT is excluded
- Start of operation: 06/2013

(1) Contribution per Member:

Planning Period	2013	2014	2015	2016	2017
Contribution / Member	5.848	22.495	19.667	26.707	24.469

(2) Research Grants:

- 30% of financing will be covered by EU grants

(3) Hosting country:

Countries hosting Common Services (Central Executive Management Office, IT Services, Stakeholder Forum, ELSI Platform, Biobank Research Services) contribute 100% of the costs for rent and investments.

(4) Personnel Costs:

The composition of the 'Common Information Technology Services' personnel is summarized in Table 10 (see chapter 10.3.3.2).

Development of 'Common Information Technology Services' personnel from 2013 to 2017:

Function	2013	2014	2015	2016	2017
Head of Informatics	0,375	0,5	0,5	1,0	1,0
Systems architect	0,25	0,5	0,5	1,0	1,0
Programmer		1,0	1,0	1,0	1,0
Developer		1,0	1,0	1,0	1,0
ICT Support Manager				1,0	1,0
Administrative support	0,25	0,5	0,5	1,0	1,0
Total FTEs	**0,875**	**3,5**	**3,5**	**6,0**	**6,0**
Number of employees	3	5	5	6	6

Function	Annual Salary
Head of Informatics	120.000
Systems architect	80.000
Programmer	75.000
Developer	75.000
ICT Support Manager	75.000
Administrative support	55.000

Annual salaries including fringe benefits

Starting salaries in 2013, annual inflation rate: 2%

(5) Investments:

Investments	period of usage (years)	Costs
Server	5	40.000
Software licensing	5	60.000
Software Updates	5	15.000

Eventually open source software will be used as much as possible, to reduce further licensing costs to a minimum after three years of operation

(6) Rent:

- 6.000 € / person /year, 25 € / sqm /month, average 20 sqm/person (including electricity, water, gas, meeting rooms), based on average rent costs in Sweden

(7) Consumables:

- 2.000 € / person /year

(8) Meetings:

- 2 meetings /year, 5.000 € / meeting

(9) Travel:

- 1000 € / trip, 3 trips per month

(10) Outsourcing:

- Some parts of the tool development will be cheaper when outsourced like e.g. the development of annotation tools for the biobank lexicon

3. *Common Service for Ethical, Legal and Societal Issues (ELSI Platform)*

Table 22 - Financial plan for the ELSI Platform from 2013 to 2017 (in EURO)

Planning Period	2013	2014	2015	2016	2017	2013 - 2017		Note
	start-up phase			full implementation				
RECEIPTS								
Member States	92.000	187.680	191.434	189.604	199.458	860.175	*77%*	(1)
Research Grants (30%)	0	0	0	87.371	91.717	179.088	*16%*	(2)
Hosting Country	26.720	13.709	13.983	14.263	14.548	83.222	*7%*	(3)
Total Financing	**118.720**	**201.389**	**205.417**	**291.238**	**305.722**	**1.122.485**	*100%*	
EXPENDITURES								
Personnel Costs	**66.250**	**135.150**	**137.853**	**220.201**	**232.723**	**792.177**	*71%*	(4)
Investments	**20.000**	**0**	**0**	**0**	**0**	**20.000**	*2%*	(5)
Other operating expenditures	**32.470**	**66.239**	**67.564**	**71.037**	**72.999**	**310.309**	*28%*	
Rent	6.720	13.709	13.983	14.263	14.548			(6)
Consumables	1.750	3.570	3.641	5.837	6.495			(7)
Travel	6.000	12.240	12.485	12.734	12.989			(8)
Meetings	10.000	20.400	20.808	21.224	21.649			(9)
Maintenance of web-tools	5.000	10.200	10.404	10.612	10.824			
Miscellaneous	3.000	6.120	6.242	6.367	6.495			
Total Costs	**118.720**	**201.389**	**205.417**	**291.238**	**305.722**	**1.122.485**	*100%*	

The financial plan for the ELSI Platform is based on the following assumptions.

- Annual rate of inflation: 2%
- VAT is excluded
- Start of operation: 07/2012

(1) Contribution per Member:

Planning Period	2013	2014	2015	2016	2017
Contribution / Member	5.288	10.010	8.752	10.922	10.239

(2) Research Grants:

- 30% of financing will be covered by EU grants

(3) Hosting country:

Countries hosting Common Services (Central Executive Management Office, IT Services, Stakeholder Forum, ELSI Platform, Biobank Research Services) contribute 100% of the costs for rent and investments.

(4) Personnel Costs:

The composition of the ELSI Platform personnel is summarized in Table 21 (see chapter 10.2.3.5)

Development of ELSI Platform personnel from 2013 to 2017:

Function	2013	2014	2015	2016	2017
Chair of Research Ethics Committee	0,25	0,5	0,5	1,0	1,0
Secretary (Chair)	0,25	0,5	0,5	1,0	1,0
Lawyer	0,25	0,5	0,5	0,5	0,5
Secretary (lawyer)	0,125	0,25	0,25	0,25	0,5
Number of FTEs	**0,875**	**1,75**	**1,75**	**2,75**	**3,00**
Number of Employees	4	4	4	4	4

Function	Annual salary
Chair of Research Ethics Committee	120.000
Secretary (Chair)	30.000
Lawyer	100.000
Secretary (lawyer)	30.000

Annual salaries including fringe benefits

Starting salaries in 2013, annual inflation rate: 2%

(5) Investments:

Investments	period of usage (years)	costs/person
Furniture	10	1.000
IT infrastructure*	5	4.000

(6) Rent:

- 3.360 € / person /year, 14 € / sqm /month, on average 20 sqm /person (including electricity, water, gas, meeting rooms)

(7) Consumables:

- 2.000 € / person /year

(8) Travel:

- 1000 € / trip, 1 trips per month

(9) Meetings:

- 2 meetings /year with at least 10 people, 10.000 € / meeting

4. *Stakeholder Forum*

Table 23 - Financial plan for the Stakeholder Forum from 2013 to 2017 (in EURO)

Planning Period	2013	2014	2015	2016	2017	2013 - 2017		Note
	start-up phase			full implementation				
RECEIPTS								
Member States	68.500	139.740	142.535	105.508	108.230	564.513	*81%*	(1)
Research Grants (30%)	0	0	0	48.367	48.722	97.090	*14%*	(2)
Hosting Country	12.520	5.141	5.244	7.348	5.455	35.708	*5%*	(3)
Total Financing	**81.020**	**144.881**	**147.778**	**161.224**	**162.408**	**697.311**	*100%*	
EXPENDITURES								
Personnel Costs	**43.750**	**89.250**	**91.035**	**100.815**	**102.831**	**427.681**	*61%*	(4)
Investments	**10.000**	**0**	**0**	**2.000**	**0**	**12.000**	*2%*	(5)
Other operating expenditures	**27.270**	**55.631**	**56.743**	**58.409**	**59.577**	**257.630**	*37%*	
Rent	2.520	5.141	5.244	5.348	5.455			(6)
Consumables	1.250	2.550	2.601	3.184	3.247			(7)
Meetings	15.000	30.600	31.212	31.836	32.473			(8)
Travel	6.000	12.240	12.485	12.734	12.989			(9)
Miscellaneous	2.500	5.100	5.202	5.306	5.412			
Total Costs	**81.020**	**144.881**	**147.778**	**161.224**	**162.408**	**697.311**	*100%*	

The financial plan for the Stakeholder Forum is based on the following assumptions.

- Annual rate of inflation: 2%
- VAT is excluded
- Start of operations: 06/2013

(1) Contribution per Member:

Planning Period	2013	2014	2015	2016	2017
Contribution / Member	4.419	8.023	7.014	6.594	6.013

(2) Research Grants:

- 30% of financing will be covered by EU grants

(3) Hosting country:

Countries hosting Common Services (Central Executive Management Office, IT Services, Stakeholder Forum, ELSI Platform, Biobank Research Services) contribute 100% of the costs for rent and investments.

(4) Personnel Costs:

The composition of the Stakeholder Forum personnel is summarized in Table 13 (see chapter 10.2.4)

Development of Stakeholder Forum personnel from 2013 to 2017:

Function	2013	2014	2015	2016	2017
Manager	0,50	1,0	1,0	1,0	1,0
Secretary	0,125	0,25	0,25	0,50	0,50
Number of FTEs	**0,625**	**1,25**	**1,25**	**1,50**	**1,50**
Number of Employees	2	2	2	2	2

Function	Annual salary
Manager	80.000
Secretary	30.000

Annual salaries including fringe benefits

Starting salaries in 2013, annual inflation rate: 2%

(5) Investments:

Investments	Period of usage (years)	Costs/person
furniture	10	1.000
IT infrastructure*	5	4.000

(6) Rent:

- 2.520 € / person /year, 14 € / sqm /month, on average 15 sqm /person (including electricity, water, gas)

(7) Consumables:

- 2.000 € / person /year

(8) Meetings:

- 2 Stakeholder meetings /year, 15.000 € / meeting, including travel costs

(9) Travel:

- 1000 € / trip, 1 trip per month

5. *Common Biobanking and Resources Services*

Table 24 - Financial plan for the Common Biobanking and Resources Services from 2013 to 2017 (in EURO)

Planning Period	2013	2014	2015	2016	2017	2013 - 2017		Note
	start-up phase			full implementation				
RECEIPTS								
Member States				188.947	197.316	386.264	*65%*	(1)
Research Grants (30%)				90.844	88.071	178.916	*30%*	(2)
Hosting Country				23.023	8.183	31.206	*5%*	(3)
Total Financing	**0**	**0**	**0**	**302.814**	**293.571**	**596.385**	*100%*	
EXPENDITURES								
Personnel Costs				**222.854**	**227.311**	**450.164**	*75,5%*	(4)
Investments				**15.000**	**0**	**15.000**	*2,5%*	(5)
Other operating expenditures				**64.961**	**66.260**	**131.221**	*22,0%*	
Rent				8.023	8.183			(6)
Consumables				6.367	6.495			(7)
Meetings				31.836	32.473			(8)
Travel				12.734	12.989			(9)
Miscellaneous				6.000	6.120			
Total Costs	**0**	**0**	**0**	**302.814**	**293.571**	**596.385**	*100%*	

The financial plan for the Common Sample and Data Access is based on the following assumptions.

- Annual rate of inflation: 2%
- VAT is excluded
- Start of operations: 01/2016

Contribution per Member:

Planning Period	2013	2014	2015	2016	2017
Contribution / Member	0	0	0	10.881	10.120

(2) Research Grants:

- 30% of financing will be covered by EU grants

(3) Hosting country:

Countries hosting Common Services (Central Executive Management Office, IT Services, Stakeholder Forum, ELSI Platform, Biobank Research Services) contribute 100% of the costs for rent and investments.

(4) Personnel Costs:

The composition of the personnel for the Common Biobanking and Resources Services is summarized in Table 9 (see chapter10.3.3.1)

Development of the personnel for Common Sample and Data Access from 2013 to 2017:

Planning Period	2013	2014	2015	2016	2017
Director	0	0	0	1,0	1,0
Secretary	0	0	0	1,0	1,0
Assistant	0	0	0	1,0	1,0
Number of FTEs	**0**	**0**	**0**	**3,00**	**3,00**
Number of Employees	0	0	0	3,0	3,0

Function	Annual salary
Director	120.000
Secretary	30.000
Assistant	60.000

Annual salaries including fringe benefits

Starting salaries in 2016, annual inflation rate: 2%

(2) Investments:

Investments	Period of usage (years)	Costs/person
Furniture	10	1.000
IT infrastructure*	5	4.000

(3) Rent:

- 2.520 € / person /year, 14 € / sqm /month, on average 15 sqm /person (including electricity, water, gas)

(4) Consumables:

- 2.000 € / person /year

(5) Meetings:

- 2 meetings /year, 15.000 € / meeting, including travel costs

(6) Travel:

- 1000 € / trip, 1 trip per month

6. *BBMRI-ERIC National Nodes*

The National Nodes are funded by the respective Member Countries. The total BBMRI-ERIC budget comprises the common BBMRI-ERIC budget as well as the budget for all National Nodes which in total account for 64% of the total BBMRI-ERIC budget (see Fig. 12).

There are minimal requirements for the set-up of the National Nodes defined to participate in BBMRI-ERIC: Each National Node will be established under BBMRI-ERIC and has to have a Director, appointed by an appropriate authority of the Member State. The National Node Director coordinates the participation of national biobanks in BBMRI-ERIC. Overall the size of the Country Nodes will depend on the complexity of the biobanking infrastructure in the respective countries.

Table 25 - Financial plan for two scenarios of National Nodes from 2013 to 2017 (in EURO)

Small National Node	**2013**	**2014**	**2015**	**2016**	**2017**	**2013 - 2017**		Note
	start-up phase			full implementation				
RECEIPTS								
Member State	195.040	188.741	192.516	196.366	200.293	972.956	*100%*	(1)
Total Financing	**195.040**	**188.741**	**192.516**	**196.366**	**200.293**	**972.956**	***100%***	
EXPENDITURES								
Personnel Costs	**150.000**	**153.000**	**156.060**	**159.181**	**162.365**	**780.606**	*80,2%*	(2)
Investments	**10.000**	**0**	**0**	**0**	**0**	**10.000**	*1,0%*	(3)
Other operating expenditures	**35.040**	**35.741**	**36.456**	**37.185**	**37.928**	**182.350**	*18,7%*	
Rent	5.040	5.141	5.244	5.348	5.455			(4)
Consumables	4.000	4.080	4.162	4.245	4.330			(5)
Travel	24.000	24.480	24.970	25.469	25.978			(6)
Miscellaneous	2.000	2.040	2.081	2.122	2.165			
Total Costs	**195.040**	**188.741**	**192.516**	**196.366**	**200.293**	**972.956**	*100%*	

Big National Node	**2013**	**2014**	**2015**	**2016**	**2017**	**2013 - 2017**		Note
	start-up phase			full implementation				
RECEIPTS								
Member States	335.080	345.862	352.779	359.834	367.031	1.760.586	*100%*	(1)
Total Financing	**335.080**	**345.862**	**352.779**	**359.834**	**367.031**	**1.760.586**	*100%*	
EXPENDITURES								
Personnel Costs	**270.000**	**275.400**	**280.908**	**286.526**	**292.257**	**1.405.091**	*79,8%*	(2)
Investments	**20.000**	**0**	**0**	**0**	**0**	**20.000**	*1,1%*	(3)
Other operating expenditures	**45.080**	**70.462**	**71.871**	**73.308**	**74.774**	**335.495**	*19,1%*	
Rent	10.080	10.282	10.487	10.697	10.911			(4)
Consumables	8.000	8.160	8.323	8.490	8.659			(5)
Travel	24.000	48.960	49.939	50.938	51.957			(6)
Miscellaneous	3.000	3.060	3.121	3.184	3.247			
Total Costs	**335.080**	**345.862**	**352.779**	**359.834**	**367.031**	**1.760.586**	*100%*	

The financial plan for the Country nodes is based on the following assumptions.

- Annual rate of inflation: 2%
- VAT is excluded
- Start of operations: 01/2013

(1) The National Nodes are funded by the respective Member Countries.

(2) Personnel Costs:

The composition National Node personnel is summarized in Table 8 (see chapter 10.3.2)

Development of National Node personnel from 2013 to 2017:

Function	2013	2014	2015	2016	2017
Director	1,0	1,0	1,0	1,0	1,0
Secretary	1,0	1,0	1,0	1,0	1,0
Additional Personnel (optional, country dependent)	2,0	2,0	2,0	2,0	2,0
Number of FTEs	**4,0**	**4,0**	**4,0**	**4,0**	**4,0**
Number of Employees	4	4	4	4	4

Function	Annual salary
Director	120.000
Secretary	30.000
Additional Personnel	60.000

Annual salaries including fringe benefits

Starting salaries in 2013, annual inflation rate: 2%

(2) Investments:

Investments	Period of usage (years)	Costs/person
Furniture	10	1.000
IT infrastructure*	5	4.000

(3) Rent:

- 2.520 € / person /year, 14 € / sqm /month, on average 15 sqm /person (including electricity, water, gas)

(4) Consumables:

- 2.000 € / person /year

(5) Travel:

- 1000 € / trip, 2 trips per month

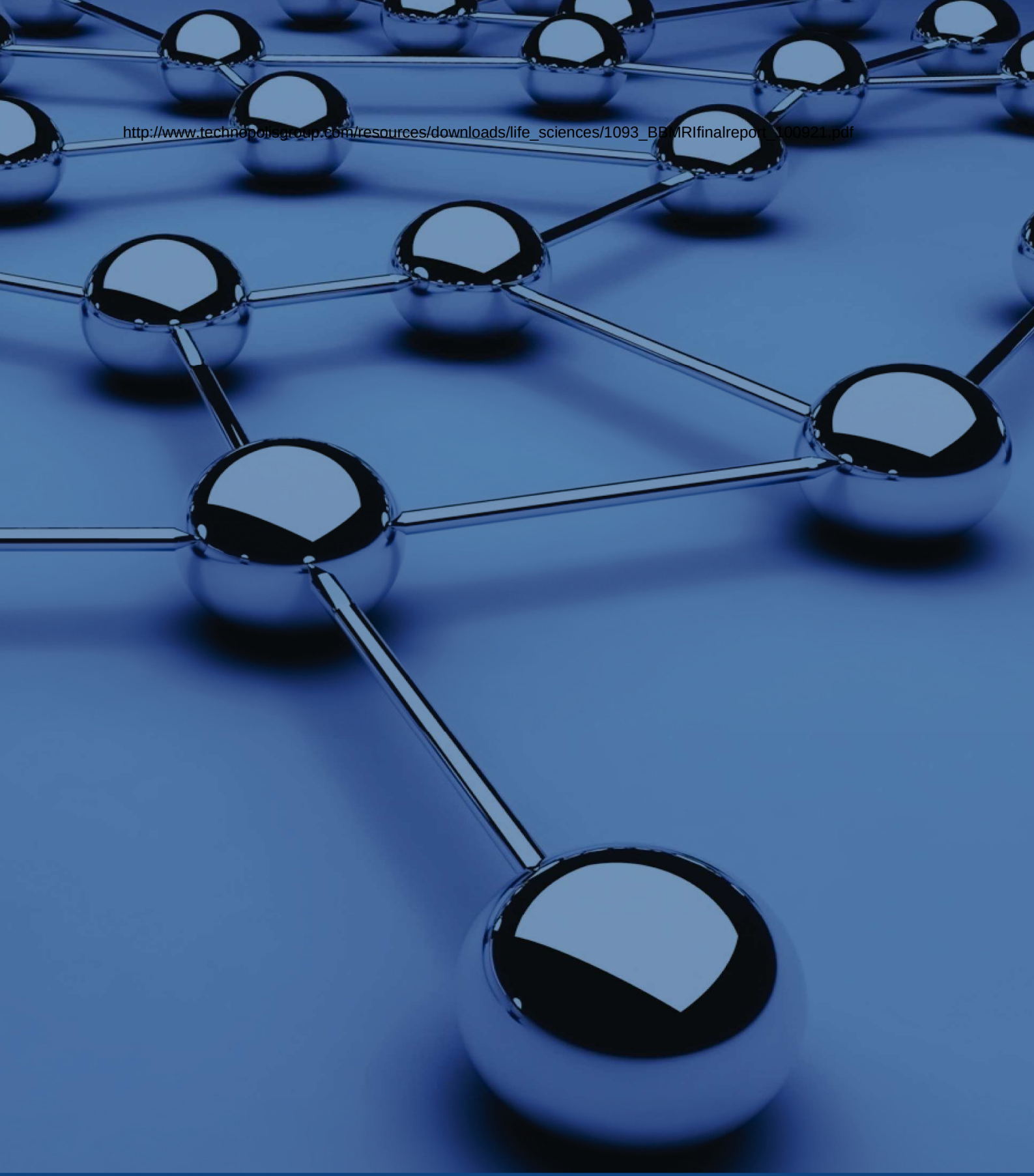
Annex VII: Summary of impact studies

Buereau d'économie théorique et appliqué. Health and Economic impact of BBMRI. Evaluation methodology and access rules of biobank networks. May 2010

The full report can be accessed at the BBMRI website:
http://www.bbmri.eu/index.php/publications-a-reports

Technopolis Group. BBMRI: an evaluation strategy for socio-economic impact assessment. September 2010

The full report can be accessed at the BBMRI website:
http://www.technopolisgroup.com/resources/downloads/life_sciences/1093_BBMRIfinalreport_100921.pdf



http://www.technopolisgroup.com/resources/downloads/life_sciences/1093_BBMRIfinalreport_100921.pdf

SEVENTH FRAMEWORK PROGRAMME