

## BBMRI

### The Pan-European research infrastructure for Biobanking and Biomolecular Resources: managing resources for the future of biomedical research



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### Summary

Biobanks are a key resource for unravelling the molecular basis of disease subtypes, identification of new targets for therapy and reduction of attrition in drug discovery and development. The broad spectrum of existing biobanks is considered as a specific strength of European research. Unfortunately the diversity - lack of standardisa-

tion - of these biobanks and the differential ethical and legal landscape across Europe have prevented their effective use. Development of common IT infrastructure and sustainable funding schemes are key features for large transnational projects interlinking different national and regional biobanks. Agreement on common standards is equally important for all *de novo* biobanks. In 2008, a pan-European infrastructure BBMRI (Biobanking and Biomolecular Resources Research Infrastructure) was established to bring cohesion to the European biobanking community and to make the existing and new high quality biological resources available for health research in Europe (Fig. 1).

### Introduction

The sequencing of the human genome, completed in the 21<sup>st</sup> century, allows researchers to integrate new data on genetic risk factors with demographic and lifestyle data collected via traditional cohort studies or via modern communication technologies. The technical prerequisites now exist in Europe for merging large volumes of molecular genetic data obtained by using new high throughput DNA analysis platforms with clinical, epidemiological and national health registry data. One of the widely recognised strengths of European research is our long-term tradition to conduct large-scale clinical and epidemiological studies and to collect biological samples from the study subjects for analyses and storage. Combined with data on nutrition, life style and environmental exposure, such longitudinal cohorts have already demonstrated their strengths [1-2]. Therefore it is not surprising that human-derived biological sample collections and related biomolecular resources were identified as one of the most promising research infrastructures in the first ESFRI (European Strategy Forum on Research Infrastructures) roadmap published in 2006 [<http://cordis.europa.eu/esfri/roadmap.htm>] [3]. In addition to BBMRI (Biobanking and Biomolecular Resources Research Infrastructure, <http://www.bbmri.eu>) five other biological and medical sciences (BMS) infrastructures were selected for the roadmap of 34 mature proposals, representing bioinformatics, structural biology, mouse biology, translational research and clinical research. Biobanked samples and information about the samples obviously provide important material also for the other BMS infrastructures.

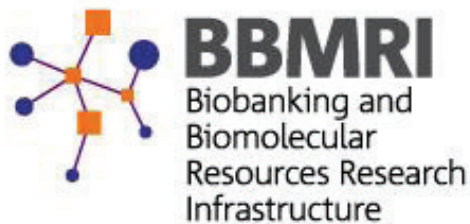


Figure 1. BBMRI logo.

Although the existing biological sample collections, biobanks and biomolecular resources are a recognised European strength, biobank-based research suffers from the characteristic European weakness – fragmentation. The samples available have been collected and stored nationally using different techniques and IT-solutions, and under different ethical and legal frameworks, which has made pan-European collaboration in large-scale projects quite challenging. Such a situation has resulted in duplication of effort in different EU Member States, although at the same time large research projects funded by the EC or other sources have demonstrated the usefulness and feasibility of collaboration between large European population-based biobanks [4-5]. Without doubt, efficient use of existing European biobanks has been hampered by their heterogeneity and lack of standardisation and has overall resulted in their underutilisation. For the study of common multifactorial diseases, a major health problem of the ageing European population, collaboration between existing national resources should create the synergism, the gain of statistical power and the economy of scale needed. The existence of population isolates is another European strength by facilitating analysis of predisposing factors in more homogeneous genetic background.

This is the landscape where BBMRI is expected and prepared to integrate the existing quality controlled biobanks, biomolecular resources and enabling technologies into a novel pan-European biomedical research infrastructure, and to guide the way towards establishment of high quality *de novo* European biobanks adhering to the guidelines drafted by BBMRI [6]. The European Commission has granted 5 Mio. € funding for 27 months (2008-2010) to the prepar-

atory phase of BBMRI to conceptualise and secure funding for the construction of the European research infrastructure for biobanking and biomolecular resources.

### The aims of BBMRI

The objectives to be addressed by the BBMRI consortium during the preparatory phase are to develop a plan to integrate existing quality controlled biobanks, biomolecular resources and enabling technologies into a novel pan-European biomedical research infrastructure. BBMRI will not only provide a comprehensive source of information about existing biological sample collections and biomolecular resources, but will also provide an operational concept for a sustainable infrastructure, deliver standard operational procedures for future biobanking and codes of conduct for European biobanks. A particularly challenge is the generation of an IT infrastructure capable of linking the existing biobank-derived genetic and molecular phenotyping data with data from clinical phenotyping and health-related registries. Furthermore, BBMRI will evaluate the heterogeneous European ethical and legal frameworks to find solutions how to implement a pan-European infrastructure, as well as to elaborate sustained funding solutions for European biobanking.

### Strategy

BBMRI will improve the accessibility and interoperability of the existing comprehensive collections of population based and disease orientated biological samples from different (sub)populations of Europe, including the attached data on health status, nutrition, lifestyle and environmental exposure of the study subjects. As the existing biobanks have a strong national character and background, a distributed hub-and-spoke structure has been suggested for BBMRI. This structure should provide great flexibility so that new members and partners can be connected at any time and the structure can be adapted to the emerging needs of biomedical research. Combined with the expertise of the clinicians, pathologists, bioinformaticians and molecular biologists involved, a globally unmatched, Europe-wide platform for translational medical research is envisaged to develop personalised medicine and disease prevention to the benefit of European citizens. 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. An important strategic goal is to create guidelines for better interoperability of *de novo* biobanks. Such guidelines should also help to overcome the current obstacle created by the heterogeneous ethical and legal landscape in Europe. In addition to clinical, ethical and legal experts, patient communities will be involved to achieve standards and guidelines which properly balance individual values, such as protection of privacy and informed consent, with shared values of facilitated access and progress in health care development and prevention.

### Action plan

The action plan of the preparatory phase BBMRI is defined in the grant agreement with the EC. The seven Work Packages (WP) of BBMRI (Table 1) are responsible for the specific deliverables aimed at integrating the existing quality controlled biobanks, biomolecular resources and enabling technologies into a novel pan-European biomedical research infrastructure. The operational concept of BBMRI for the next stage will be developed based on the experience gained during the preparatory phase. The distributed hub-and-spoke structure will facilitate generation of technological platforms in areas such as biological resources, high-throughput techniques, bioinformatics and other advanced analytical tools for data analysis. Such platforms will also foster collaboration between academia and industry.

Hubs are coordinated and directed by an executive management, which is supported by a governance council as well as by a scientific and ethical advisory board and receives input from the stakeholder forum (Fig. 2). The IT infrastructure which employs a federated database architecture will integrate the complex network of hubs, members and associated partners.

One of the challenges of setting up large scale studies is the heterogeneous legal and ethical frameworks within the EU. The new European legal entity (ERIC) that is currently being developed by the European Commission particularly to support the needs and operation of research infrastructures, foresees the establishment of operational sites in different Member States under one legislation. Such an entity would provide an outstanding opportunity to generate an integrated and harmonized biomedical research area and joint policies for legal and ethical frameworks within the EU. If ERIC is delayed, an interim solution for a legal entity (an international society or an association) will be considered.

### Successes

All work packages started their work in February 2008 although funding from the EC only became available in June 2008. Due to the large size of the project the management and organizational structure may appear complex, but has shown its effectiveness in practice. The three-level management structure provides an open and transparent decision-making process which can also be applied for the implementation stage of BBMRI.

Table 1. BBMRI Work Packages (WP's) and governance structure and leaders/chairs.

Work Packages (WP)	Leader(s)
<b>WP1:</b> Management and Coordination	K. Zatloukal (AT), E. Vuorio (FI)
<b>WP2:</b> Population-based Biobanks	L. Peltonen (FI/UK), A. Metspalu (EE)
<b>WP3:</b> Disease-orientated Biobanks	E. Wichmann, (DE), T. Meitinger (DE)
<b>WP4:</b> Biomolecular Resources and Molecular Tools	U. Landegren (SE), M. Taussig (UK)
<b>WP5:</b> Database harmonisation and IT-infrastructure	J-E. Litton (SE), M. Fransson (SE)
<b>WP6:</b> Ethical, Legal and Societal Issues	A. Chambon-Thomsen (FR)
<b>WP7:</b> Funding and Financing	G. Dagher (FR), J. Ridder (NL) C. Brechot (FR)
Governance Council Chair	L. Peltonen (FI/UK)
Advisory Board Chair	G-J. van Ommen (NL)
Coordination Board Chair	K. Zatloukal (AT)
Stakeholder Forum Chair	M. Griffith (IR)

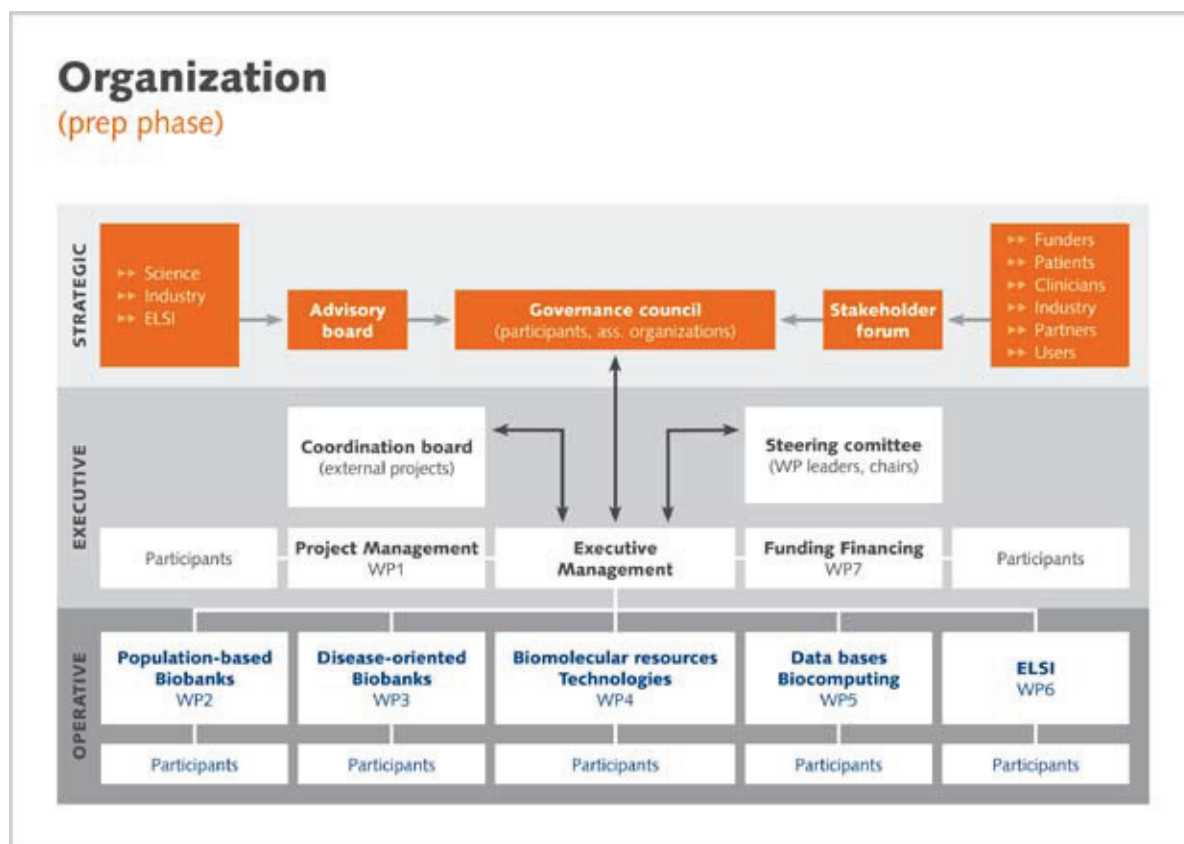


Figure 2. BBMRI organisation and responsibilities.

Initially the EU-funded BBMRI preparatory phase project comprised 50 participants and about 150 associated organisations from 24 countries. One indication of the increased visibility and acceptance of BBMRI is the fact that within the first year the number of associated organisations has increased to 190 representing 29 European countries (Fig. 3). Partners of BBMRI have placed major emphasis on the proper embedding of BBMRI in the global biobanking community. Political and public recognition of BBMRI has increased through presentations in the European Parliament and in a large number of journals and public media. Work on biobank harmonization is coordinated with the P<sup>3</sup>G consortium (The Public Population Project in Genomics, [www.p3gconsortium.org](http://www.p3gconsortium.org)), the strategic research agenda of the Innovative Medicines Initiatives (IMI), the WHO, and the OECD initiative on a global network of Biological Resource Centres. Key representatives of these projects and initiatives have contributed to the goals of the preparatory phase as participants in work packages, members in various boards or as external experts.

One of the early tasks of BBMRI was to prepare an inventory of existing population-based (WP2) and clinical (or disease-orientated, WP3) biobanks in Europe using a survey questionnaire based on an existing P<sup>3</sup>G questionnaire. This core questionnaire was supplemented with a total of ten supplementary questionnaires dealing with issues such as standardization of procedures, data collection and handling, IT solutions as well as legal and ethical issues and funding. Data obtained from the survey has been added to the BBMRI web site, but additional information is expected to be collected by the WPs throughout the preparatory phase.

WP4 has reviewed existing resources for affinity reagents and other biomolecular resources as analytical tools applicable to biobanking. This has led to a new community standard of affinity reagents (MIAPAR) (submitted for publication), designed to tackle the problems of scattered information and imprecise descriptions and facilitate database implementation. In addition, a new database for molecular methods (MoIMeth, [www.molmeth.org](http://www.molmeth.org)) [7-8] has been established,





Figure 3. BBMRI Participants and associated organisations. Participants are co-applicants of the project and full members. They have an official vote on formal issues in the Governance Council that is responsible for the definition of the appropriate strategy and processes, and is required for the approval of reports and any changes of the work plan. Associated Members do not have an official vote, but they receiving all relevant information on BBMRI (e.g. forthcoming events, achievements, media reports) and they have the right to participate in several activities, such as Work Package meetings and the BBMRI Governance Council meeting.

providing best practice-based protocols for molecular analyses of different types of samples. Key to any large assembly of data, be it biological, clinical, epidemiological, or behavioral, is the system for information management. WP5 coordinates and supervises all processes of the IT, informatics and infrastructure in the project. Success has been made in finding consensus on a general information management system for maintaining unique and secure coding systems for specimens, subjects and biobanks. WP5 has initiated a searchable BBMRI catalogue of disease-oriented biobanks together with WP3. The catalogue provides a high-level description of Europe's biobanks, including contact details, background and objectives, descriptions of available samples and data and the possibilities for access according to informed consent, links to the biobanks websites etc.

Analyses on the ethical, social and legal issues of the infrastructure have resulted in a conceptual paper on ethics related policies for biobanks and biomolecular resources. Furthermore, a WIKI+ platform for legal aspects of biobanks has been designed and presented as planned. The

next step will be its launch on the project website and the involvement of experts.

WP7 has progressed with the challenging tasks of surveying the current and prospective financial needs of biobanks in order to develop a sustainable funding concept for BBMRI. In addition to support from the EC, the biobanks participating in the BBMRI preparatory phase have received commitment from 23 research and health ministries and funding agencies in 13 different European countries. Successful negotiations for sustainable funding for joint BBMRI activities form a critical and vitally important effort as the future of BBMRI is dependent on an efficient central unit coordinating all key activities of the pan-European biobank and biomolecular resource.

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## EATRIS

### Infrastructure bridges Basic Research and Medical Innovation



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The “European Advanced Translational Research InfraStructure in Medicine”, EATRIS, is a new research infrastructure initiative which will help Europe to fulfil its potential in the strategically critical area of translational medical research. EATRIS is a unique framework linking European countries to accelerate the development of new medicinal products by facilitating access to a new pan-European infrastructure. EATRIS is one of the biomedical infrastructure projects initiated by the European Strategy Forum on Research Infrastructure (ESFRI) and is currently funded by the 7<sup>th</sup> Framework Programme of the European Commission.

#### Translational Medicine

“Translational medical research” or “translational medicine” is the crucial step between basic laboratory research and practical, clinical applications. At its best, translational medicine is a two-way street: the discoveries of basic research are developed into new tools for clinical care, and observations made in clinical care can inspire new approaches in basic research (Figure 1).

Everywhere in Europe basic researchers are hitting the same obstacles: they explore disease mechanisms, they find ways to influence these mechanisms and find new targets. They find ways to influence the target. All this contributes to the understanding of the biology of human disease. But the next step, the practical application of their basic work and the advancement into preclinical and clinical trials, is not available