COMBINATION OF COLLABORATIVE PROJECTS AND COORDINATION AND SUPPORT ACTIONS FOR INTEGRATING ACTIVITIES

FP7-INFRASTRUCTURES

Support to existing research infrastructures

INFRA-2010-1.1.12:
Large-scale bio-banks for clinical and epidemiological studies.

Data Integration and Access Logistics for the Biobanking and Biomolecular Resources Infrastructure

DIAL-BBMRI

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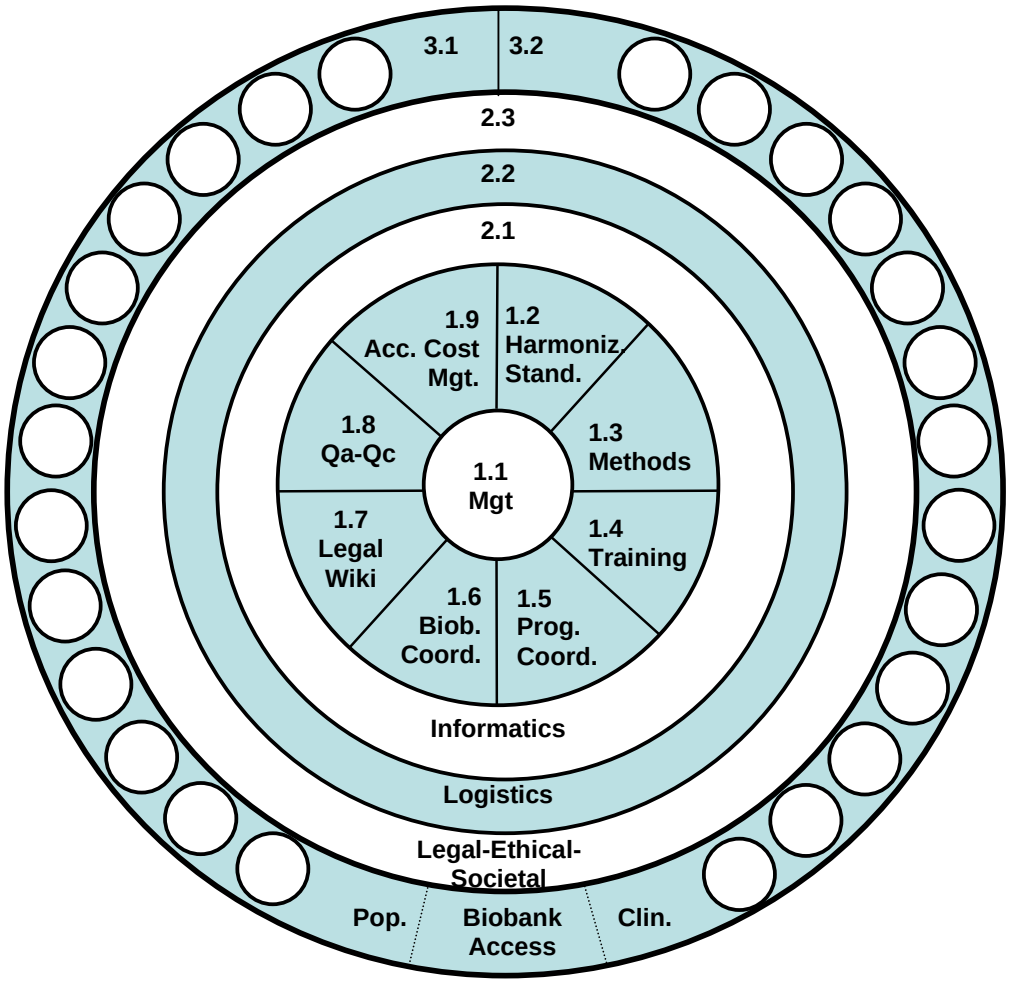

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Proposal

1: Scientific and/or technical quality, relevant to the topics addressed by the call

1.1 Concept and objectives

Human biological samples including associated medical data, and biomolecular research tools are a key resource in unravelling the interplay of genetic and environmental factors causing diseases and impact on their outcome, identification of new targets for therapy and reduction of attrition in drug discovery and development. In 2007, the pan-European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) has been established in its 'preparatory phase' to prepare for integrating existing sample collections, resources, technologies, and expertise, to prepare for later extension and complementation with innovative components, properly embedded into European scientific, ethical, legal and societal frameworks. Sustainability will be achieved stepwise by funding and financing solutions appropriate to the subsequent stages in the growth trajectory of this European-wide, distributed infrastructure. BBMRI will increase the scientific excellence and efficacy of European research in the biomedical sciences as well as expand and secure competitiveness of European research and industry in a global context and attract back (investments in) pharmaceutical and biomedical research facilities (from outside Europe).

In this preparative phase, until medio 2010, BBMRI has provided, and will extend and consolidate:

- Biobanks of different formats (based on collections of DNA, tissue, cells, blood and other body fluids, together with pertinent medical, environmental, life-style and follow-up data)
  - Population cohorts, including prospective and twin cohorts
  - Clinical case/control cohorts including disease-focused cohorts
  - Cohorts from isolated populations
- Biomolecular resources (comprising antibody and affinity binder collections, ORF clone collections, siRNA libraries, proteins, cellular resources etc.)
- An inventory of enabling technologies and high-throughput analysis platforms and integration of sites specialized in development of molecular tools to decipher gene, protein and metabolite functions and their interactions
- The first steps towards harmonized standards for sample collection, storage, and analysis, in close coordination with previous and parallel activities like the worldwide P3G programme
- The first steps towards harmonized data collection, logistics and database- and biocomputing infrastructure
- An inventory of the ethical, legal and societal landscape in Europe, with an outlook towards providing guidance towards future harmonization of regulations.

The work during BBMRI-PP built on previous and ongoing national, European and global projects and initiatives, such as research projects funded under FP5 and FP6 as well as new projects under FP7, public/private partnerships (PPPs) which are directly related to the needs of BBMRI, work on biobank harmonization done by the P^3G and PHOEBE consortia, the strategic research agenda of the Innovative Medicines Initiatives, the WHO, and the OECD initiative on a global network of Biological Resource Centres. The basic BBMRI-PP principle has been one of subsidiarity: integrating and harmonizing biomolecular resources and molecular tools with complementary national and regional biobank formats, each with its own strengths, to render their combination much more powerful than each resource type alone.

In the next period, the BBMRI community aims to ensure that the quality and clinical annotation of biological samples, as well as their accessibility to the user community, meets the requirements of current and future analysis tools. This will provide the best research opportunities to define and correlate healthy, pre-clinical and clinical profiles, and will strongly boost the integrated study of biological and genetic disease mechanisms, improve the delineation of clinical phenotypes and establish biomarker spectra for disease prognosis and therapy monitoring. If properly funded in the impending construction phase, BBMRI can be stabilized and extended into a major resource of wide strategic and practical utility, both in the biomedical arena and – through pioneering work in biospecimen storage and provision – also in the wider field of the life sciences. This will give European scientists, industry and citizens distinct advantages, such as

- broad and unified access to the catalogued information on biological samples and collected data, which before the emergence of BBMRI was cumbersome and due to different, fragmented data structures and incompatible regulations for their access and exchange in different countries,

- a setting to establish an open-source (code) based federated database structure that can guarantee the same standard of data quality in annotation while protecting donors' privacy,
- a structure to provide access to a Europe-wide data and sample set for investigators thus providing data with better statistical power or permitting the investigation of rare or highly diverse diseases,
- capacity and code of conducts to develop prospective collections meeting the needs of particular research projects or clinical trails, based on Europe-wide networking of biobanks meeting compatible quality standards,
- compliance with, as well as further constructive alignment of, ethical and legal requirements,
- sound governance system building on input by all stakeholders,
- ultimately, a solid funding scheme for up keeping and updating of the resources.

In order to make a smooth transition from the preparatory phase to the construction phase of a pan-European Biobanking Infrastructure, it should be realized that the biobank landscape in Europe, as it was – and still is - inventorized by BBMRI, is extremely diverse. On one hand there are large, regionally and nationally well-established facilities, often population-oriented, with a long history and a high publication track record, and also smaller, but equally well-established and -organized clinical biobanks with great, disease-specific information depth. On the other hand there is a great variety of smaller biobanks, maintained in hospitals by clinical experts with a specific focus or research question, often on a voluntary basis and with a more fragmented funding history. A recent development - in part caused by the member states' attention for the ESFRI process and the impact of BBMRI in this context – has been the targeting of major national funds towards the establishment of newly conceived, large and well-equipped biobank. There can be transversal and population-based, like Biobank-UK, or clinically-oriented and prospective, like the Dutch Pearl String Initiative.

Considering these field dynamics, it was deemed appropriate to focus the next step in the BBMRI establishment on the enlisting of the key, large-scale European biobanks, i.e. the mature parties who have also played a trailblazing role in the BBMRI-PP, in the delivery of a proof-of-principle to provide widespread access of interested users to their data and samples. This optimally fits the present call under the FP7-INFRASTRUCTURES heading, which has as one of its aims to 'provide support to existing research infrastructures' in the form of a 'combination of collaborative projects and coordination and support actions for integrating activities'. Specifically, this proposal in is response to the topic: **INFRA-2010-1.1.12: 'Large-scale biobanks for clinical and epidemiological studies'.**

The main goals specified under this heading are

- to provide access to samples and data for clinical and epidemiological studies.
- to enhance cataloguing (e.g. of samples, tools and methods),
- to develop tools for enhancing access to data and samples,
- to address the harmonisation of Ethical, Legal and Social Issues (ELSI).
- that such a project will be structured in coordination with the ESFRI "BBMRI" project.

The aim of this present proposal is to fulfil exactly the above mentioned goals. It is optimally served by focusing on the more advanced biobanks and the BBMRI core community, who are well-integrated in the BBMRI infrastructure as established in the Preparatory Phase. They can serve as a prototype which can later be extended, with additional funding of mainly national but also pan-European nature, to expand the access logistics once it has achieved a robust format, informatically, technologically and ethically, as explored and implemented through the present I3 call.

1.2 Progress beyond the state-of-the-art

The DIAL-BBMRI proposal builds on the work done within the BBMRI preparatory phase (PP) and consists of three interrelated packages of activities. The provision of access to data and samples in Biobanks require the integration of several coordination activities, the innovative development of informatics tools, technologies and the advancing of a legal, ethical and societal framework, all to underpin the access provision in a proper framework which is sustainable in the future of Europe's research and development agenda. For the short term future a legal structure is foreseen for BBMRI under the ERIC legal entity (BBMRI-ERIC) and serves as a proof-of-concept for accessing BBMRI resources and services. Because of this intimate relationship a good coordination of both projects (DIAL-BBMRI and BBMRI-PP) is essential. Furthermore, BBMRI-PP has

important synergies with other biological and medical sciences (BMS) research infrastructures of the ESFRI road map and takes care of the biobanking-related issues for all other BMS infrastructures. Furthermore, BBMRI-PP coordinates a joint communication task force and prepares a joint white paper to be presented to the European Parliament in 2010. These synergies should be considered in procedures established within DIAL-BBMRI. Rules and procedures of BBMRI-PP build on the OECD best practice guidelines for biological resource centres, which define key issues for transnational access, quality assurance, safety and security. This provides also a common basis for transnational sample and data access from/for resource centres in OECD Member or partner states outside of Europe and establishing efficient global collaboration. Compatibility with global initiatives is also facilitated by the fact that BBMRI-PP recommends the WHO/IARC guidelines for biological resource centres as templates for internationally harmonized SOPs.

DIAL-BBMRI project will take European collection of biological resources to a new level of coordination and efficiency, providing new services and better access for users. it aims to provide a one-stop access to the collections of the European biobanking community, expertise and services via a searchable web portal, building on the outcome of BBMRI project preparatory phase. DIAL-BBMRI not only aims to foster access to the European academic community, but also to other parties like the health care system and the private sector. The latter will typically take shape as public-private partnerships, to allay potential concerns of data and sample security and public availability of the results obtained with public funding. The access provided will be based on proper peer review and ethical assessment of research proposals, as well as on the existing and allowed policies of the biobanks.

To achieve this aim DIAL-BBMRI will:

- Develop a procedure to prioritize requests to samples and associated data
- Study the possibilities to encourage biobanks to keep an adequate supply of specimens to keep up with customer/researcher demand.
- Develop SOP and appropriate tools to increase support for the resource and investment in the quality of the resources collected and their associated data.
- Harmonize cost assessment to resources, associated data and access to services and expertise.
- Implement appropriate methodology and indicators to assess the accrual of distribution to public and private partners and the impact of DIAL-BBMRI on socioeconomic issues.

Improved data and greater access to a wider range and better maintained resources as proposed by DIAL-BBMRI will provide European academic and industrial with a huge advantage over the rest of the world and a road to delivering the bioeconomy.
The structure of the presently proposed work is summarized as follows:

1.2.1 Management

The infrastructure of DIAL BBMRI foresees a central work package devoted to the management and coordination of the programme as a whole, followed by three strata of activities – This is Work Programme 1.1

1.2.2 Networking activities

A series of defined coordination activities, each of which constitutes as a work package, as follows.

- Harmonization and standardization - WP1.2
- Molecular tools and technologies -WP1.3
- Training and dissemination - WP1.4
- Strategic health programme coordination - WP1.5
- Global biobanking coordination - WP1.6
- Provision of a WIKI legal platform - WP1.7
- Quality management - WP1.8
- Cost assessment and monitoring - WP1.9

Brief description

These coordinating work packages address a series of different, but interlinked activities, necessary to lay the ground work of current-day, comprehensive biobank operations. They address issues of correlating different nomenclatures, phenotyping standards, thus improving data interoperability; cataloguing the scattered molecular

tools and technologies; contributing to human capacity building and improving the understanding amongst the wider public, industry, and academia; coordinating our developments with the many other heath initiatives and organisations, as well as amongst the different worldwide biobanking initiatives themselves, providing guidance to the legal community and governmental decision makers; maintaining up to date standards of materials and data quality; and keeping track of cost developments in this rapidly innovating field.

These work packages require a greatly diverse expertise, located in a decentral fashion throughout Europe. This is why our proposal may have a higher number of participants than usual for a central research facility which aims to provide transnational access to a defined scientific resource and connected expertise, as is typically the case with large physics resources. The DIAL-BBMRI Work Packages are operated in parallel as relatively small, networked activities, by well-known European experts from the BBMRI community, and further strengthened by overseas expertise from the P3G community. Their outcome will be integrated at regular Annual General Meetings and more frequent exchanges by topical meetings and teleconferences. Moreover, the personal unions between these different work packages warrant an ongoing exchange of advances in insights at work-package specific meetings and teleconferences. See for a detailed description the tabular format of the work packages.

1.2.3. Joint research activities

The products of the coordination work packages will provide continuous input to the next step in building the infrastructure: the further advancement of tools, technologies and legal-ethical-societal insights. This part comprises the RTD activities and is the 'innovative engine' of the DIAL-BBMRI programme, aimed at furthering insight into these issues, and translating these insights into the development of enabling procedures and logistics for the actual data and sample access provision. Each of the three branches in this section constitutes an RTD work package with the corresponding focus:

- Biobank Informatics – WP2.1
- Biobanking technology and logistics – WP2.2
- Legal, ethical and societal positions – WP 2.3

Brief description

Like for the networking activities, these work packages are operated in parallel as distributed activities, by well-known European experts who are closely-knit because this community is not very large. In this case, however, there is a strong research and technology innovation focus, reflected by a major role by a leading expert in the field.

Notably the biobanking informatics is a field which is in high demand and rapid flux. The tasks ahead for this group are of a substantial multiplicity:

- developing better solutions for secure storage, retrieval and analysis of an exponentially growing body of sample data and clinical annotations – fundamentally decentral because of biobank regulations, but yet to be presented as seamlessly as possible for collated browsing and analysis
- improving user interfaces in view of the mission to provide access to a broader user community
- addressing – for the first time in a systematic fashion – the linguistic complexity of free format clinical and data annotation in the many European languages.

All of these issues are addressed, which explains the relative funding magnitude of this key development area.

Also the biobanking technology and logistics is a key development field. The size of the sample sets is greatly increasing due to a major ramping-up of national biobank investments. This requires assessment, recommendations and decisions concerning advanced protocols and systems for storage and retrieval, data capture, technical quality maintenance and inventorizing and adapting to user needs.

The development of legal, ethical and societal positions is the third key activity essential in assisting the biobanking infrastructure with fulfilling its role. Life sciences and biotechnology are commonly seen as major fields having a central role in the knowledge society of the near future. Improving cross-communication between societal disciplines and aligning the regulatory frameworks will be a prime opportunity to improve communication, foster better understanding, and prevent misunderstanding. The biobanking arena, with its complex regulatory, ethical and societal landscape across Europe, has the chance of spearheading innovation and greatly contributing to the debate: both between the scientific, medical, legislative and social disciplines, and between the professionals, the patient communities and the public at large. This is why the BBMRI-PP has

already enlisted, early on, the diverse stakeholder community, into a specific Stakeholder Forum. This function will be continued and strengthened in the DIAL-BBMRI phase.

1.2.4 Transnational access activities.

As an infrastructure, DIAL-BBMRI is not a unique localized, central physical unit where researcher can have access to costly instrumentation or highly specialized research activities. The uniqueness lies in the scientific value of access to biological samples, clinical measurements, questionnaire data on exposure and personal health information often collected through repetitive screening based health surveys. Transnational access to samples will therefore be the major asset and transnational activities should subsequently stimulate the development of an optimal, state-of-the-art national infrastructure to promote the best quality of samples.

Due to a different degree of homogeneity and logistical issues, the final access work package has been subdivided into two sections:

- Access to population biobank data and samples – WP 3.1
- Access to clinical biobank data and samples – WP3.2

In practice, the infrastructure offered to the European research community through DIAL-BBMRI, will be spread over a large number of European countries and has a notable diversity in terms of physical localisation, sample handling procedures, internal logistics as well as degree of automation. However, there is a major convergence process ongoing throughout Europe, driven by the availability, recent or impending, of significant national funds for collating and converging the biobanking activities in several member states, while others are in the early stages of a similar process. Indeed, the establishment of BBMRI-PP has been an important catalyst in this process. Thus, the structuring and harmonizing of the prototype biobanks to improve sample handling efficiency, a significant activity in the DIAL-BBMRI phase, has already received substantial tailwind in several leading member states. The ground has been prepared for the development of common access rules for all biobank prototypes, both population based and clinical. Obviously, but specifically stated here it will be assured, in collaboration with WP 1.7 and WP 2.3, that access procedures and sample management are in compliance with the existing ethical and legal requirements

Starting out from an initial global assessment – achieved within BBMRI-PP by extensive consultation of the parties and finalised at a two-day prototype meeting on December 1-2, 2009 - a correct pricing system will be further developed to provide both sustainability of the selected prototype biobanks as well as promoting access from research groups. The dominating income will be based on access fee to samples or analysis derived from samples. The costs for a straight forward sample refinement as DNA-isolation and normalization will not vary much, and the unit cost of access may be set without a complicated system for price estimation. The uncertainty lies in the number of researchers applying for access. The challenges lies in securing stable and comparable sample quality, strongly focused. In collaboration with WP 1.2, WP 2.2 and WP 3.2 we will develop, harmonize and implement best practices/best quality for collection, processing, annotation, storage, and distribution protocols to ensure the highest quality samples and comparability of research results.
A common access portal and the implementation of a common IT-infrastructure will be amongst DIAL-BBMRI's products, accessible via the BBMRI web site Development of a common web based inventory and a catalogue for presentation of meta data will also have high priority.

1.3 S/T methodology and associated work plan

1.3.1 Overall Strategy

The integral coherence of the work packages in the different sections (management, networking, RTD, and access) has been described above.
The coherence between the different sections is ensured by the personal unions of participants in different work packages, through the internal section of the website and at the annual general meetings and other conferences, like the stakeholder and user conferences. The ultimate deliverables of the programme are the samples and data provided and the research enabled through this, although this latter will fall beyond the actual project period. The stakeholder and user conferences are main deliverables to optimally guide the access provision according to the needs of the user community, where the central management, coordination activities, the research and technology development activities and the experiences gathered from previous access activities come together with the interest of the patient groups and the user community. In the deliverables list these deliverables are connected to several work packages.
The flow of the process is depicted in figure 1 below, with the management at the core, surrounded by the eight coordination work packages, providing and receiving input from the three RTD packages, to ultimately feed into the access work packages, which constitute the interface to the user community and the public at large.

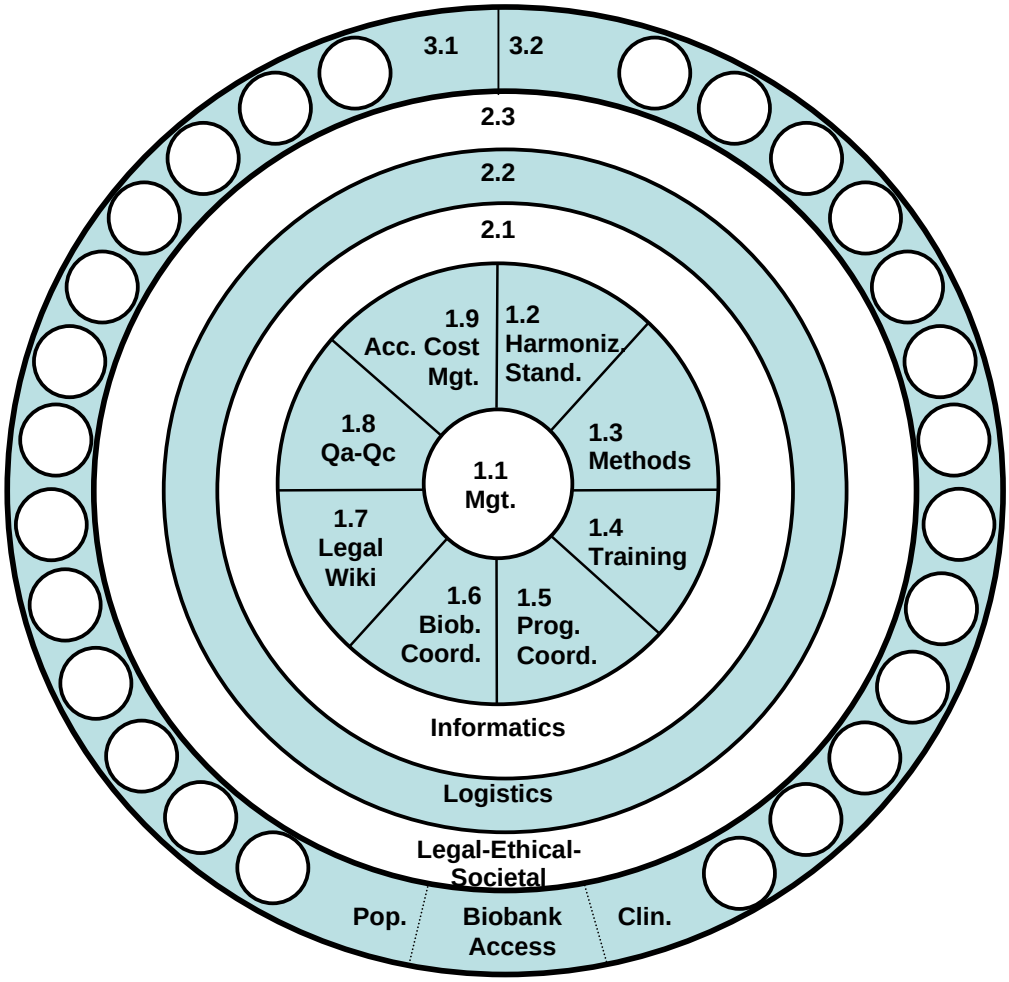

Figure 1: Diagram of operational structure

GANTT CHART

D nr.	Deliverable name	Year 1				Year 2				Year 3				Year 4			
D1.1.1	Release of web-site																
D1.1.2	Information package (flyer, brochure)																
D1.1.3	General annual reports																
D1.1.4	Joint stakeholder/user conferences and publication of procedure on web site																
D1.1.5	Mid term report																
D1.1.6	Final report																
D1.1.7	User Access report																
D1.2.1	Preliminary report on outstanding challenges in harmonization, standardization and calibration to be presented at first DIAL-BBMRI annual conference																
D1.2.2.	Repository of methods and tools for harmonization, standardization and calibration in biobanking goes live on P3G Observatory and is mirrored to BBMRI web site																
D1.2.3.	Demonstrate repository of methods and tools for harmonization, standardization and calibration in biobanking at second DIAL-BBMRI annual conference																
D1.2.4.	Present proposals to respond to outstanding challenges in harmonization, standardization and calibration to third DIAL-BBMRI annual conference																
D1.2.5.	Present final report on response to outstanding challenges in harmonization, standardization and calibration to fourth DIAL-BBMRI annual conference																
D1.3.1	Database of binding reagents for analysis of biobanked samples and of European resource centres providing relevant services.																
D1.3.2	Database of methods for analysis of biobanked samples																
D1.3.3	Web portal for resources and molecular technologies applicable to biobanked samples																
D1.4.1	Project website																
D1.4.2	Patient Organization Training Workshop																
D1.4.3	Three international biobanking training courses																
D1.4.3	European biobanking training agenda																
D1.4.4	PR material																
D 1.5.1	Cross reference in web sites																
D 1.5.2	Joint stakeholder/user conferences and publication of procedure on web site																
D 1.5.3	Joint Steering Committee meetings																
D 1.5.4	Workshop with non-European biological resource centres																
D 1.5.5	Workshop with IMI-EFPIA representatives and IMI-coordinators																
D1.6.1	Identify key initiatives to interface with																
D1.6.2	Develop a strategic integration plan for systematic and regular inter-project communication																
D1.6.3	Develop a strategic horizon scanning plan for the science and the societal issues																
D1.6.4.	Meet every 6 months with relevant projects and produce an overview report of the key coordination and scanning aspects																
D.1.7.1	National Templates first version public																
D.1.7.2	European Cross Border Templates first version public																
D.1.7.3	Updates and upgrades of legal documents																
D1.7.4	Full version of Wiki Legal Platform																
D1.7.5	Final version of Wiki Legal Platform																
D1.8.1	Workshop with biobank personnel and report on best practices																
D1.8.2	Workshop with biobank personnel and report on quality control of resources																
D1.8.3	Seminar or summer school on quality assurance																
D 1.9.1	Joint stakeholder/user conferences and publication of procedure on web site																

D 1.9.2	Workshop with non-European biological resources centres and report on access costs																		
D1.9.3	Report on accrual of distribution and socio-economic indicators																		
D2.1.1	Biobank informatics activity-specific project plan																		
D2.1.2	Joint report on Data Protection with work packages 1.7 and 2.3																		
D2.1.3	Roadmap and reports for project collaborations																		
D2.1.4	Test report of integrating IT applications into the BBMRI PP prototype																		
D2.1.5	Extended requirements specification, comprising the results of the consensus process for the core and the extended data sets																		
D2.1.6	Test of implemented services, improvement of service implementations, and refinement of the service architecture, with specific regard to security and test of the biobank toolkit																		
D2.1.7	Refinement of the federated schema																		
D2.1.8	Results of impending terminology mapping services in relation to Activity 2.1.3																		
D2.1.9	Preparation of online user-guide (describing installation and operation of client software), roll-out																		
D2.1.10	ConceptWiki Biobank version																		
D2.1.11	Design, description and implementation of the user interface																		
D2.1.12	Design, description and implementation of an interactive tagging system																		
D2.1.13	Design, description and implementation of analysis tools																		
D.2.2.1	Exploring existing and desired technological solutions.																		
D 2.2.2	Explore the diversity and specific requirements related to older biobank collections. Scientific report																		
D 2.2.3	Sample handling and access procedures. Descriptive report																		
D 2.2.4	Strategic development studies on biobanking technology: Scientific report																		
D 2.2.5	Descriptive scientific reports from data capture task, with tentative recommendations and design of pilot studies for evaluation of biomarkers of quality.																		
D 2.2.6	Strategic joint research projects on biobanking per se. Scientific reports																		
D 2.2.7	Dissemination of knowledge detailing the results of tasks 1-8. Scientific reports																		
D2.3.1	Set up working groups and precise methodology on the various aspects of WP2.3																		
D2.3.2	Position paper on biobank access policies and policy options for biobank infrastructure. (ACCESShaper)																		
D2.3.3	Points to consider paper on biobanking children samples and data in a networked environment of biobanks																		
D2.3.4	Report on cord blood biobanking for research in Europe and table comparing stem cell/cord blood banking with population/genetic biobanking and research																		
D2.3.5	General Report on attitudes in EU countries from the Eurobarometer survey																		
D2.3.6	Country reports on attitudes of EU citizens following focus groups																		
D2.3.7	Cross analysis of attitudes of EU citizens following focus groups and Eurobarometer																		
D2.3.8	Position paper on the communication of results and findings to various publics																		
D2.3.9	Final position paper on governance policies for biobanking infrastructure																		
D2.3.10	Overall report on ELSI research																		
D.3.1	Common national BBMRI biobank infrastructure for sample handling																		
D.3.2	Common access rules to public biobanks, population based and clinical.																		
D.3.3	Ethical and legal requirements for access																		
D.3.4	Prizing of samples and costs of access																		
D.3.5	Common web based solutions for access and a dynamic inventory of storage																		
D. 3.1	QA/QC on best practices																		
D. 3.7	Inventory, structuring of metadata																		

Table 1.3 a: Work package list

Work package No	Work package title	Type of activity	Lead partici-pant nr	Lead participant short name	Person-months	Start month	End month	Indicative Total costs	Indicative requested EC contribution
WP1.1	***Management***	MGT	1	LUMC	186	1	48	2,084,160	2,084,160
WP1.2	***Harmonization/standardization***	COORD	10	ULEI	36	1	48	184,147	184,147
WP1.3	***Molecular tools and technologies***	COORD	13	BBT	44	1	48	223,523	223,523
WP1.4	***Training and dissemination***	COORD	8	IPRI	102	1	48	710,694	710,694
WP1.5	***Strategic health programme coordination***	COORD	2	MedUG	56	1	48	282,587	282,587
WP1.6	***Global biobanking coordination***	COORD	15	NIPH	44	1	48	231,548	231,548
WP1.7	***WIKI legal platform***	COORD	14	LP	17	1	48	308,909	308,909
WP1.8	***Quality management***	COORD	9	UniMAN	24	1	48	125,083	125,083
WP1.9	***Access and cost management***	COORD	5	INSERM	24	1	48	125,083	125,083
WP2.1	***Biobank Informatics***	RTD	11	KI	336	1	48	2,635,093	1,976,320
WP2.2	***Biobanking technology and logistics***	RTD	3	NTNU	36	1	48	283,093	212,320
WP2.3	***Legal, ethical and societal positions***	RTD	5	INSERM	60	1	48	430,667	323,000
WP3.1	***Population biobank data, sample access***	SUPP	3	NTNU	100	1	48	1,508,250	1,508,250
WP3.2	***Clinical biobank data, sample access***	SUPP	12	HMGU	132	1	48	1,665,754	1,665,754
		TOTAL			**1197**			**10,886,852**	**9,990,884**

Table 1.3 b1: Deliverables List

Del. no.[1]	Deliverable name	WP no.	Nature[2]	Dissemination level[3]	Delivery date[4](mo)
D1.1.1	Release of web-site	1.1	P	PU	2
D1.1.2	Information package (flyer, brochure)	1.1	O	PU	8
D1.1.3	General annual reports	1.1, all	R	RE	13, 25, 37, 48
D1.1.4	Joint Stakeholder and User conferences and publication of proceedings on web site	1.1 1.5 1.9	O, R	RE	14, 32
D1.1.5	Mid term report	1.1	R	RE	26
D1.1.6	Final report	1.1	R	RE	48
D1.1.7	User Access report	1.1	R	PU	48
D1.2.1	Preliminary report on outstanding challenges in harmonization, standardization and calibration to be presented at first DIAL-BBMRI annual conference	1.2	R	PU	12
D1.2.2.	Repository of methods and tools for harmonization, standardization and calibration in biobanking goes live on P3G Observatory and is mirrored to BBMRI web site	1.2	D	PU	24
D1.2.3.	Demonstrate repository of methods and tools for harmonization, standardization and calibration in biobanking at second DIAL-BBMRI annual conference	1.2	D	PU	24
D1.2.4.	Present proposals to respond to outstanding challenges in harmonization, standardization and calibration to third DIAL-BBMRI annual conference	1.2	O	RE	36

[1] Deliverable numbers in order of delivery dates. Please use the numbering convention <WP number>.<number of deliverable within that WP>. For example, deliverable 4.2 would be the second deliverable from work package 4.

[2] Please indicate the nature of the deliverable using one of the following codes:
R = Report, **P** = Prototype, **D** = Demonstrator, **O** = Other

[3] Please indicate the dissemination level using one of the following codes:
PU = Public
PP = Restricted to other programme participants (including the Commission Services).
RE = Restricted to a group specified by the consortium (including the Commission Services).
CO = Confidential, only for members of the consortium (including the Commission Services).

[4] Measured in months from the project start date (month 1).

D1.2.5.	Present final report on response to outstanding challenges in harmonization, standardization and calibration to fourth DIAL-BBMRI annual conference	1.2	R	PU	48
D1.3.1	Database of binding reagents for analysis of biobanked samples and of European resource centres providing relevant services.	1.3	P	PU	36
D1.3.2	Database of methods for analysis of biobanked samples	1.3	P	PU	48
D1.3.3	Web portal for resources and molecular technologies applicable to biobanked samples	1.3	P	PU	24
D1.4.1	Project website	1.4	P	PU	6
D1.4.2	Patient Organization Training Workshop	1.4	O	RE	18
D1.4.3	Three international biobanking training courses	1.4	O	PU	18, 30, 42
D1.4.3	European biobanking training agenda	1.4	R	PU	24
D1.4.4	PR material	1.4	O	PU	12-48
D 1.5.1	Cross reference in web sites	1.5	0	PU	3
D 1.5.2	Joint stakeholder/user conferences and publication of proceedings on web site	1.1 1.5 1.9	0	PU	14, 32
D 1.5.3	Joint Steering Committee meetings	1.5	0	RE	36
D 1.5.4	Workshop with non-European biological resource centres	1.5	0	PU	24
D 1.5.5	Workshop with IMI-EFPIA representatives and IMI-coordinators	1.5	0	RE	20
D1.6.1	Identify key initiatives to interface with	1.6	R	PU	3
D1.6.2	Develop a strategic integration plan for systematic and regular inter-project communication	1.6	R	PP	6
D1.6.3	Develop a strategic horizon scanning plan for the science and the societal issues	1.6	R	RE	12
D1.6.4.	Meet every 6 months with relevant projects and produce an overview report of the key coordination and scanning aspects	1.6	R	RE	6-48

D.1.7.1	National Templates first version public	1.7	O	PU	2
D.1.7.2	European Cross Border Templates first version public	1.7	O	PU	6
D.1.7.3	Updates and upgrades of legal documents	1.7	O	PU	2-47
D1.7.4	Full version of Wiki Legal Platform	1.7	O	PU	2
D1.7.5	Final version of Wiki Legal Platform	1.7	O	PU	48
D1.8.1	Workshop with biobank personnel and report on best practices	1.8	O	RE	18
D1.8.2	Workshop with biobank personnel and report on quality control of resources	1.8	O	RE	24
D1.8.3	Seminar or summer school on quality assurance	1.8	O	RE	12
D 1.9.1	Joint stakeholder/user conferences and publication of proceedings on web site	1.9	O	PU	14, 32
D 1.9.2	Workshop with non-European biological resources centres and report on access costs (mo 20)	1.9	O/R	PU	18-20
D 1.9.3	Report on accrual of distribution and socio-economic indicators	1.9	R	PU	24
D2.1.1	Biobank informatics activity-specific project plan	2.1	R	PP	3
D2.1.2	Joint report on Data Protection with work packages 1.7 and 2.3	2.1 1.7 2.3	R	PP	36
D2.1.3	Roadmap and reports for project collaborations	2.1	R	PP	12-48
D2.1.4	Test report of integrating IT applications into the BBMRI PP prototype	2.1	R	PP	6
D2.1.5	Extended requirements specification, comprising the results of the consensus process for the core and the extended data sets	2.1	R	PP	12
D2.1.6	Test of implemented services, improvement of service implementations, and refinement of the service architecture, with specific regard to security and test of the biobank toolkit	2.1	R,P	PP	24

D2.1.7	Refinement of the federated schema	2.1	R	PP	18
D2.1.8	Results of impending terminology mapping services in relation to Activity 2.1.3	2.1	R	PP	36
D2.1.9	Preparation of online user-guide (describing installation and operation of client software), roll-out	2.1	P	PP	48
D2.1.10	ConceptWiki Biobank version	2.1	P	PU	6
D2.1.11	Design, description and implementation of the user interface	2.1	P	PU	9
D2.1.12	Design, description and implementation of an interactive tagging system	2.1	P	PP/PU	18
D2.1.13	Design, description and implementation of analysis tools	2.1	P	PP/PU	36
D.2.2.1	Exploring existing and desired technological solutions.	2.2	R	RE	18
D 2.2.2	Explore the diversity and specific requirements related to older biobank collections. Scientific report	2.2	R	RE	24
D 2.2.3	Sample handling and access procedures. Descriptive report	2.2	O/R	RE	36
D 2.2.4	Strategic development studies on biobanking technology: Scientific report	2.2	O/R	RE	42
D 2.2.5	Descriptive scientific reports from data capture task, with tentative recommendations and design of pilot studies for evaluation of biomarkers of quality. Scientific reports	2.2	R	RE	36
D 2.2.6	Strategic joint research projects on biobanking per se. Scientific reports	2.2	R	RE/PU	48
D 2.2.7	Dissemination of knowledge detailing the results of tasks 1-8. Scientific reports	2.2	R	RE/PU	48
D2.3.1	Set up working groups and precise methodology on the various aspects of WP2.3	2.3	R	PU	4
D2.3.2	Position paper on biobank access policies and policy options for biobank infrastructure. (ACCESShaper)	2.3	R	PU	24
D2.3.3	Points to consider paper on biobanking children samples and data in a networked	2.3	R	PU	12

	environment of biobanks				
D2.3.4	Report on cord blood biobanking for research in Europe and table comparing stem cell/cord blood banking with population/genetic biobanking and research	2.3	R	PU	30
D2.3.5	General Report on attitudes in EU countries from the Eurobarometer survey	2.3	R	PU	12
D2.3.6	Country reports on attitudes of EU citizens following focus groups	2.3	R	PU	24
D2.3.7	Cross analysis of attitudes of EU citizens following focus groups and Eurobarometer	2.3	R	PU	30
D2.3.8	Position paper on the communication of results and findings to various publics	2.3	R	PU	36
D2.3.9	Final position paper on governance policies for biobanking infrastructure	2.3	R	PU	42
D2.3.10	Overall report on ELSI research	2.3	R	PU	48
Common for WP 3.1 and WP 3.2					
D.3.1	Common national BBMRI biobank infrastructure for sample handling	3.1	P	PU	48
D.3.2	Common access rules to public biobanks, population based and clinical.	3.1	R	RE	24
D.3.3	Ethical and legal requirements for access	3.1	R	PP	24
D.3.4	Prizing of samples and costs of access	3.1	R	RE	36
D.3.5	Common web based solutions for access and a dynamic inventory of storage	3.1	O/R	RE	48
D. 3.6	QA/QC on best practices	3.1	R	RE	48
D. 3.7	Inventory, structuring of metadata	3.1	O	RE/PU	38

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Table 1.3 b2: Summary of transnational access provision

Participant number	Organisation short name	Short name of infrastructure	Installation		Operator	Unit of access	Estimated unit cost (€)	Min. quantity of access to be provided	Estimated number of users	Estimated number of projects
			Number[1]	Short name	country code[2]					
2	MedUG	Prototype Austria	2		Austria	Clinical biobank	5000 € per project*,	Samples and data**	30-40	36 in 4 y
19	EGP	Prototype Estonia	1		Estonia	Population biobank	5000 € per project*,	Samples and data**	30-40	36 in 4 y
7	THL	Prototype Finland	1		Finland	Population biobank	5000 € per project*,	Samples and data**	30-40	36 in 4 y
5	INSERM	Prototype France	2		France	clinical biobank	5000 € per project*,	Samples and data**	30-40	36 in 4 y
12	HMGU	Prototype Germany	1+2	KORA	Germany	Population + clinical biobank	5000 € per project*,	Samples and data**	30-40	36 in 4 y
28	ISS	Prototype Italy	2		Italy	clinical biobank	5000 € per project*,	Samples and data**	30-40	36 in 4 y
1	LUMC	Prototype Netherlands	1+2	Life Lines	Netherlands	Population + clinical biobank	5000 € per project*,	Samples and data**	30-40	40 in 4 y
3	NTNU	Prototype Norway	1	HUNT	Norway	Population biobank	5000 € per project*,	Samples and data,	30-40	36 in 4 y
20	USAL	Prototype Spain	1+2		Spain	Population + clinical biobank	5000 € per project*,	Samples and data**	30-40	36 in 4 y
11	KI	Prototype Sweden	1	KI biobank	Sweden	Population biobank	5000 € per project*,	Samples and data**	30-40	36 in 4 y
9	UNIMAN	Prototype UK	1+2	CIGMR	Prototype UK	Population + clinical biobank	5000 € per project*,	Samples and data**	30-40	36 in 4 y
Sum		**All 11 national prototypes**					**5000t€ per project*, 2 000 000 € in total**	**Samples and data****	**330-440**	**400 in 4 y**

1 Number progressively the installations of a same infrastructure. An installation is a part of an *infrastructure* that could be used independently from the rest.

2 Give the country code of the operator of the infrastructure or INO if the operator is an international organization.

Table 1.3 c: List of milestones

Milestone number	*Milestone name*	*Work package involved*	*Expected date [1] (mo)*	*Means of verification[2]*
M 1.1.1	Employment of project manager	1.1	1	Project manager working
M 1.1.2	Establishment of all boards	1.1	1-3	Board members announced in minutes
M 1.1.3	Release of web-site	1.1	2	Web-site in the air
M 1.1.4	Annual general meetings	1.1	3, 15, 27, 39, 47	Minutes
M 1.1.5	WP progress reports	1.1	12, 24, 36, 47	Reports
M 1.1.6	Stakeholder and User conferences	1.1, 1,5	14, 32	Meeting, meeting reports
M.1.2.1	The issues selected for prioritization of D1.2.4	1.2	36	Realization of D1.2.5
M1.3.1	Prototype database of methods for analysis of biobanked samples deployed on the web.	1.3	12	Feedback from stakeholders/users tracking progress of the new tools created.
M1.3.2	Prototype web portal for resources and molecular technologies publicly available.	1.3	12	Evaluation report of functionality and usability by the user community
M1.3.3	Prototype database of binding reagents and European resource centres public and deployed on the web	1.3	18	Survey of database functionality and usability by the user community
M1.3.4	Database of methods for analysis of biobanked samples fully deployed on the web	1.3	36	Database released and validated by the user community
M1.4.1	Initiation of a European Master and/or PhD programme	1.4	24	Press release
M1.4.2	Working group set-up	1.4	4	Minutes
M1.4.3	Biobanking training course curriculum advertisement	1.4	8	Publication
M1.4.4	Dissemination report	1.4	48	Report
M 1.5.1	Stakeholder and User conferences	1.5	14, 32	Meeting, meeting reports
M1.6.1	Within-project information compilation from WP leaders	All	2	Summary list sent to coordinator
M1.6.2	Develop template for strategic integration plan	1.6	4	Template for comment circulated within WP
M1.6.3	Develop method for strategic horizon	1.6	5	Overview report describing

[1] Measured in months from the project start date (month 1).

[2] Show how you will confirm that the milestone has been attained. Refer to indicators if appropriate. For example: a laboratory prototype completed and running flawlessly; software released and validated by a user group; field survey complete and data quality validated.

	scanning and identify individuals focusing on the science and on the societal aspects of this.			approach and identifying individual's involved by area of focus
M1.6.4	Meeting dates, agendas and participants, minutes, action items	1.6	6-48	Log of meeting dates, agendas, participants, minutes and action items
M1.6.1	Within-project information compilation from WP leaders	All	2	Summary list sent to coordinator
M.1.7.1:	Establishment of Network of National Correspondents	1.7	1-24	Confirmation of terms and conditions; publication on platform
M.1.7.2	Establishment of Wiki Editorial Board	1.7	3	Confirmations in writing; publication of Editorial Board Rules of Procedure on Platform
M.1.7.3	Identification and development of links with compatible platforms and projects	1.7	12-48	Links on Platform. Joint meeting with PI's of compatible platforms and projects
M.1.8.1	Collect information on best practices and quality control	1.8, 1.9, 3.1, 3.2	9	Guidelines
M.1.8.2	Develop and common Guidelines	1.8, 3.1, 3.2	12	Report
M.1.8.3	Seminar or summer school	1.8 , 3.1, 3.2	14	Participant assessments
M.1.9.1	Information on cost of samples	1.9, 3.1, 3.2	10	Report
M.1.9.2	Implement indicators in biobanks	1.9	8	Report
M.1.9.3	Publish access procedure	1.9, 2.3, 3.1, 3.2	12	Publication on web site[2] and other support
M.1.9.4	Workshop access cost	1.9, 2.3, 3.1, 3.2	20	Workshop, report
M.1.9.5	Accrual of distribution and socio economic indicators	1.9, 3.1, 3.2	24	Report
M 2.1.1	Project plan	2.1	3	Report
M 2.1.2	ConceptWiki Biobank	2.1	6	Publication
M 2.1.3	Roadmap and extended requirements specification	2.1	12	Report; Dissemination among participating centres
M 2.1.4	Implementation of service architecture	2.1	24	Successful tests; Press release
M 2.1.5	Joint report on data protection	1.7, 2.1, 2,3	36	Report
M 2.1.6	ConceptWiki implementation	2.1	36	Press release
M2.2.1	International conference on technologies and biobanking	2.2, 3.1, 3.2	3	Workshop report
M2.2.2	Status of existing clinical biobank collections	2.2, 3.1, 3.2	18	Analysis of questionnaires
M2.2.3	State-of-the- art sample handling and access procedures	2.2, 3.1, 3.2	18	Intermediate report
M2.2.4	Strategic development studies on	2.2, 3.1,3.2	24	Project plans designed

	biobanking technology			based on data in D1-D3
M2.2.5	Uniform markers of sample quality	1.8, 2.2, 3.1, 3.2	24	Intermediate reports
M2.3.1	Studies on biobanking strategies per se	1.8, 2.1, 3.1, 3.2	42	Critical review of study results List available
M2.3.2	International conference on the technology of biobanking Access to Eurobarometer results secured	1.8, 2.1, 2.2, 3.1, 3.2, 1.9	42	Conference report File available
M2.3.3	Mechanism for discussion/approval position papers	2.3	10	Procedure available to Project steering board
M2.3.4	Teams in place for focus groups ready	2.3	12	Intermediate report by task leader
M2.3.5	Consultation process among stakeholders in place	2.3	18	Procedure available to Project steering board
M2.3.6	Calendar to prepare integration of the various dimensions agreed upon	2.3	25	Approved minutes
M2.3.7	Input from prototype available	2.3	36	Compilation of comments available (WP leader)
M2.3.8	Parameters of governance agreed upon	2.3	40	Approved minutes (WP leader)
Common for WP 31 and WP 3.2				
M3.1	Agreement reached on common biobank infrastructure logistics for sample access	2,2, 3.1, 3.2,	12	Signed agreement
M3.2	Consensus on access rules	1.2, 3.1, 3.2,	12	Signed agreement
M3.3	Developed a common set of ethical an legal guidelines	1.7, 3.1, 3,2	12	Guidelines
M3.4	Developing a minimal set of a common prizing system	1.1, 3.1, , 3.2	12	Price list
M3.5	Completion of first prototype of an a web based access portal	2.1, 3..1, 3.2	18	Web portal prototype
M3.6	Collect information of existing quality standards	1.2, 3.1, 3.2	24	Report
M3.7	Agreement on structure of common inventory/Meta data catalogue	2.1, 3.1, 3.2	36	Work group report

Tables 1.3 d1: Work package descriptions

Work package 1.1

Work package number	1.1	**Start date or starting event:**		Mo 1		
Work package title	***Management***					
Activity Type	MGT					
Participant number	**1**	**2**	**3**	**4**	**5**	**6**
Participant short name	LUMC	MedUG	NTNU	UTU	INSERM	WTSI
Person-months per participant:	72	4	4	36	4	12
Participant number	**7**	**8**	**9**	**10**	**11**	**12**
Participant short name	THL	IPRI	UniMAN	ULEIC	KI	HMGU
Person-months per participant:	4	4	4	4	4	4
Participant number	**13**	**15**	**19**	**24**		
Participant short name	BBT	NIPH	UTARTU	IPPOSI		
Person-months per participant:	4	4	4	18		

Objectives

WP1 coordinates and supervises all processes of the project. It is responsible for reporting to the EU, and coordinates and supervises all contract negotiations. In particular, WP1 organizes the annual general meetings, the meetings and teleconferences of the project steering board, the scientific and ethical advisory board and stakeholder and user meetings, prepares documents for and reports of these meetings, and is responsible for public relations. Furthermore, it coordinates the activities of DIAL-BBMRI with that of other external projects and takes care of proper integration of DIAL-BBMRI in the global context

Description of work

Overall management

The **Executive Management** is responsible for the day-to-day integrative management and for deploying the necessary management procedures and tools. It is composed of the Project Coordinator, the Project Manager and their team members. The EM will plan, monitor and take the necessary actions to coordinate the different Work Packages and ensure successful progress. In regular consultation with the Project Steering Board, a proper balance will be maintained between robust execution of the programme as planned and leaving enough flexibility to include innovative ideas and refrain from outdated activities in the light of advancing insights. In this light, resource management will be aimed at balancing research freedom and creativity versus efficiency and a focus on results and applications. In this process, regular advice will be sought from the Scientific and Ethical Advisory Board and the Stakeholder Forum, and integrated into the work programme. Lastly, communication will have a critical role in the management structure, as outlined in section 2.1. This will be managed in close coordination with WP 1.4. Finally, it will assist the Sample and Data Access Committee in the selection process of proposals for sample and/or data access

Work Package management:

All the work will be managed at WP level by Work Package Leaders (WPL) assisted by the MT. More specifically, WPL are responsible for:

- leading the Work Package and supervising the technical and managerial activities,
- monitoring and reporting the progress of tasks and the efficiency with which they are executed,
- identifying needs for IP management,
- ensuring that WP milestones and deliverables are completed,
- organising special meetings if necessary
- Monitoring and progress reporting

Every twelve months, each WPL will submit a consolidated **WP Progress Report** to the Coordinator including the relevant managerial information (resources, costs, scheduling, etc.) The measurable progress made toward deliverables and milestones in each task will also be reported in terms of percentage of completion, estimated time remaining for completion, actual person-months spent and person-months needed to complete the task. The operational management team will consolidate the WP information and finalise a **General Annual Report** for the project. The management team will also update the bar chart and the spreadsheets tallying person-months using the data received from the WPL

The WP Progress Reports and the General Annual Reports contain:

- an overview of the activities carried out during the reporting period,
- the progress in relation to the project objectives,
- the progress towards the milestones and deliverables set for the period,
- any problems encountered and corrective actions taken.
- a detailed justification of the costs incurred and of the resources deployed by each participant.

The reports will be consolidated and submitted to the EC by the Coordinator.

A **Mid term report** will be prepared and delivered by the Coordinator, containing an overview of the work conducted in the first part of the project and the corresponding results. It will also detail what is still to be realised to achieve the goals of the project.

At the end of the project**, a Final report** will be prepared and delivered, containing an overview of the main work conducted and the results obtained throughout the entirety of the project,

In addition, also at the end of the project, a **User Access Report** will be submitted , containing**:**

- A summary of the user access
- An overview of the feedback by the users
- A forward look towards further implementation and expansion

Deliverables

D1.1.1: Release of web-site (mo2)

D1.1.2: Information package (flyer, brochure) (mo8)

D1.1.3: General annual reports (mo13, 25, 37, 48)

D1.1.4: Stakeholder and User conferences (mo14, 32)

D1.1.5: Mid term report (mo26)

D1.1.6: Final report (mo48)

D1.1.7: User Access report (mo48)

Milestones

M1.1.1: Employment of project manager (mo1)

M1.1.2: Establishment of all boards (mo1-3)

M1.1.3: Release of web-site (mo2)

M1.1.4: Annual general meetings (mo 3, 15, 27, 39, 47)

M1.1.5: WP progress reports (mo12, 24, 36, 47)

M1.1.6: Stakeholder and User conferences (mo14, 32)

Work package 1.2

WP no.	1.2			Start date or starting event:			Mo. 1			
WP title	Harmonization/standardization/calibration of data and samples									
Activity type	COORD									
Participant no.	10	9	12	15	27					
Short name	ULEIC	UniMan	HMGU	NIPH	P3G					
PM per participant	12	4	4	4	12					

Objectives

1. To consider the primary sources of information for a major bioclinical study (e.g. questionnaires, physical measures, biosamples, and electronic registries) and - for each source individually - identify, characterise and document important outstanding gaps and challenges in the field of bioclinical harmonization, standardization and calibration.

2. To construct a comprehensive information repository documenting approaches and tools that may be used in the harmonization, standardization and calibration of biobank derived information from each different source. The repository will be constructed on the website of the P³G Observatory, and mirrored on the BBMRI website.

3. To demonstrate the repository to researchers in BBMRI, and to ensure dissemination of relevant information throughout the network.

4. To prioritise the outstanding challenges identified under objective 1, in the light of pre-existing approaches and tools, under objective 2. To work with the BBMRI network and external experts to prioritise and to draw up realistic strategic plans to address those challenges that are potentially tractable.

5. To present proposals under objective 4 to researchers in BBMRI. To work with BBMRI and with external experts to determine how to respond to the prioritised proposals. This may, for example, include the undertaking of pilot work in preparation for a later grant application and/or the development of some form of harmonization/standardization/calibration support structure for BBMRI.

Description of work

Work will be undertaken in small groups centred in Leicester, Montreal, Manchester, Oslo and Munich. Links between these groups will be maintained by regular teleconferences and face-to-face workshops at DIAL-BBMRI, BBMRI and P³G conferences. The funding in each centre will be split between the provision of short-term, part-time salaries and associated costs for research assistants, support for the networking of the senior scientists, and the holding, where necessary, of focused expert workshops.

In the Biobanking field, a critical distinction must be made between standardization, harmonization, and calibration. Our definitions of these terms are as follows:

Standardization

The application of a set of procedures, rules, tools and/or systems that are the same in each of a series of studies or biobanks. Standardization restricts design flexibility but it guarantees reliable interoperability.

Harmonization

The application of a set of procedures, rules, tools and/or systems that promote - both now and in the future - the effective interchange of valid information and samples between a number of studies or biobanks, accepting that there may be important differences between those studies. In the epidemiological setting, a given study may be said to be "harmonized" for a specific variable, if that variable can be constructed using the data items that were collected in the given study (e.g. from questions in a questionnaire, physical measures and/or from the results of the analysis of biosamples) and that despite any loss of information in this process, the constructed variable is "fit for purpose" in the particular scientific context that applies. Harmonization is context specific.

Calibration

The use a function (algebraic or logical) to map the observed values of a data item collected in one way by one biobank, to the corresponding values of a related data item collected in a different way by a different biobank, or to values of a corresponding standard (e.g. to a DataSHaPER) variable. If any of the problems identified under objective 1 demand a response involving calibration, it is likely that a grant application will ultimately required to generate the calibration functions required. Pilot work will then be required to explore the pros and cons of alternative approaches to calibration, and different designs for a calibration study (see task 5).

The work program in WP1.2 is based on five tasks, and builds heavily on prior achievements. Thus, substantial international progress has already been made in the development of methods and tools to assist researchers to harmonize and standardize biobanks and bioclinical studies. This includes important contributions from BBMRI, P3G and PHOEBE, including the DataSHaPER which forms the methodological basis of BioSHaRE-EU - a complementary research-oriented application submitted by several members of our consortium in response to the FP7 Health call "Harmonisation of phenotyping and biosampling for human large-scale research biobanks" (HEALTH 2010.1.1-1). In brief, the logical flow of the work, as reflected in the specific tasks outlined is to: (1) review pre-existing progress in the field of harmonization, standardization and calibration and to identify outstanding gaps and challenges; (2) to construct a comprehensive information repository that details the current state of the art to provide a resource for researchers; (3) to demonstrate and disseminate the resource through the BBMRI consortium; (4) to work with relevant experts to develop strategic responses to the gaps and challenges identified in the first step; (5) undertake a work program to advance the realization of the strategic responses identified in the fourth step.

Task 1. We will review the current state-of-the-art in order to identify important outstanding gaps and challenges in the field of bioclinical harmonization, standardization and calibration. That is, we will identify gaps and challenges that cannot presently be addressed by the application of pre-existing approaches and tools. Task 1 will be carried out by the WP members and support staff in the five designated centres, in collaboration with multidisciplinary experts from across the BBMRI network. Where necessary external experts will also be contacted and involved, making full use of the extensive network of international researchers in almost all relevant domains that are available via the BBMRI and P3G consortia. Key challenges will be reviewed and identified independently for each primary information source (e.g. questionnaires, physical measures, biosamples, and electronic registries).

Task 2. Work undertaken in Task 1 will provide a foundation for the construction of a comprehensive repository documenting key information (see objective 2) about the approaches and tools that may be used in the harmonization, standardization and calibration of biobank derived information. The repository will be structured (as under task 1) so that approaches and tools are considered separately for each of the primary information sources. In each case, we will describe the approaches that may be used, their infrastructural and other requirements, their theoretical and practical strengths and weaknesses, and any outstanding gaps and challenges identified under task 1. Where possible, we will identify and describe at least one case-study illustrating their implementation and use, and identify experts that may be used as sources of reference for each approach. The information repository will be built on the P3G Observatory. This will enable us to take full advantage of the IT systems and structures of the Biobank-101 project. Biobank-101 is a general purpose support and guidance tool being developed by P3G to assist biobanking professionals to understand and respond to all key issues underpinning the design, construction and management of a contemporary biobank or major bioclinical study. The specific repository to be constructed under task 2 of WP1.2 of DIAL-BBMRI may therefore be viewed as a specialist "Harmonization-101" tool that will focus specifically on harmonization, standardization and calibration; both tools will be mirrored on the BBMRI website.

Task 3. Demonstrate the Harmonization-101 tool to the BBMRI consortium, and ensure that relevant information is disseminated widely throughout the network. This task will involve direct one-to-one contact between WP members and scientists in the BBMRI consortium, and presentations at DIAL-BBMRI, BBMRI and P3G conferences. Where appropriate, formal peer-reviewed publications will also be prepared, in order to disseminate knowledge and information externally.

Task 4. Members of WP1.2 will work with external experts and members of the BBMRI consortium to prioritise the outstanding gaps and challenges identified under task 1, and to develop strategic responses to these issues. Final prioritisation will take place after discussion at the third annual DIAL-BBMRI conference (see deliverable 1.2.4 and milestone 1.2.1). The work under this task will be structured in a manner corresponding to the successful approach adopted in developing the DataSHaPER. Work will be undertaken by the scientific leaders and support staff in each of the centres, with external expertise being sought (from within BBMRI and P3G, and externally) on a one-to-one basis and via small focused workshops aimed at resolving, or reaching

consensus on, key issues.

Task 5. The issues viewed as being of top priority under task 4, will provide a milestone that will determine the actual work to be undertaken under task 5. The basic program under task 5 will be organised in the same way as that under task 4, but its precise nature will therefore depend on the milestone at the end of task 4. At this stage it is anticipated that two potential lines of work under task 5 might involve: (1) the undertaking of pilot work in preparation for a later grant application (e.g. to design and conduct a European calibration study that will enable us to generate calibration functions for a range of key measures, that can then be used in biobanks not only across Europe, but also where appropriate across the world); or (2) the development of some form of support/helpdesk system to complement the Harmonization-101 repository, to assist BBMRI consortium members in harmonization, standardization and calibration.

Deliverables

D1.2.1 Preliminary report on outstanding challenges in harmonization, standardization and calibration to be presented at first DIAL-BBMRI annual conference (12 months)

D1.2.2. Repository of methods and tools for harmonization, standardization and calibration in biobanking goes live on P3G Observatory and is mirrored to BBMRI web site (24 months)

D1.2.3. Demonstrate repository of methods and tools for harmonization, standardization and calibration in biobanking at second DIAL-BBMRI annual conference (24 months)

D1.2.4. Present proposals to respond to outstanding challenges in harmonization, standardization and calibration to third DIAL-BBMRI annual conference (36 months)

D1.2.5. Present final report on response to outstanding gaps and challenges in harmonization, standardization and calibration to third DIAL-BBMRI annual conference (48 months)

References

http://www.p3gobservatory.org/datashaper/presentation.htm

Work package 1.3

Work package number	1.3	Start date or starting event:		Mo.1			
Work package title	*Molecular tools and technologies*						
Activity Type	COORD						
Participant number	13	1	22	23			
Participant short name	BBT	LUMC	UU	SLU			
Person-months per participant:	24	4	8	8			

Objectives

It is clearly important that a biobanking programme is complemented by the analysis and cataloguing of available reagents and methods, as well as of future needs. Leading examples of emerging technologies with profound impact on biobanking include next-generation DNA sequencing and mass spectrometry proteomics. These and other methods link directly to elucidation of genetic risk identifiers and biomarker identification, a central part of personalised medicine, diagnostics and therapies. Based on rapid progress in genomics and proteomics, biomedical research has generated a huge demand for biomolecular resources, but several critical issues in European biomolecular resources prevent their maximum utilisation. They include the absence of a coordinated system of information that describes specific attributes of the biological reagents; open and straightforward access to reagents and methods; and assessment of the quality of existing resources and reagents, which are in many cases incomplete and poorly controlled. Any distribution scheme requires stringent QC and validation procedures, particularly critical in the area of binding reagents, where up to 50% of commercial products are of dubious performance quality, leading to incorrect or variable experimental findings, with major cost implications and adverse impact on downstream research. Cataloguing of reagents and methods and their description in databases, generating a robust platform with open access, reagent rationalisation and data integration, is therefore of primary importance, to allow comparison between separate research efforts and metastudies based on related investigations. Ideally, the methods for analysis that will be used over the lifetime of biobanks should also guide collection and storage of the samples.

Description of work

WP1.3 aims to unite existing biomolecular resources, technologies, standards and know-how into the operational framework of BBMRI, and in so doing to provide the essential molecular tools for interrogation of biobanked samples. The scope includes collections of antibodies and related reagents, proteins and DNA ORF clones, together with methods, molecular tools and high-throughput analysis platforms for sample analysis to investigate genes, proteins and metabolites in biobanked samples.

The ultimate aim is that, for the large majority of genes, access information will be provided to a clone, a protein, a set of binding agents, and technologies for their analyses. To achieve this, resource information must first be catalogued and made available through public web pages and databases, such as the existing BBMRI resources web portal for reagents and bioinformatics, and the MolMeths database for molecular methods, both of which have been established during the BBMRI PP (WP4). Additional tasks will include recommendations for standardisation, quality control (QC) and optimisation of tools and reagents. Together, these activities will enable improved access to standardised, well validated reagents and methods, increased opportunity for research cohesion and integration, and greater reliability in comparison of results.

Relevant tasks to be undertaken within BBMRI to improve the position of European biomolecular resources are to establish databases and a web-based portal as an information site for available reagents, tools and methods relevant to biobanked samples; to develop agreed QC standards for reagents and their use; and to work closely with other initiatives promoting each of these activities. In WP1.3, expert groups will be established comprising representatives of research centres and resource providers, to ensure proper involvement of the scientific community, industry and other stakeholder groups. IP rights attached to some of the resources and technologies, and their possible cost and access implications, will also be considered thoroughly.

Prior activities

In regard to creation of a methods collection, the design and implementation of a molecular methods database MolMeth (www.molmeth.org) has been progressed substantially. MolMeth is a structured database with the aim of providing best practice protocols for molecular analyses of different types of samples to all BBMRI members and beyond (1). The database will also include protocols for sampling procedures and storage conditions. The

database is currently at the beta stage being amended in response to community feedback. Unlike commercial activities (e.g. CSH and Nature Protocols) the database is open access without user charge and fully searchable. It is possible to connect to it using web-services technology.
A web portal for biomolecular resources is under construction (http://www.bbmri-wp4.eu/) and will be available initially as a test site during year 2 of the preparatory phase. It will include links to inventories of available binder reagent resources and molecular technologies for interrogating biobank samples at the DNA, protein and metabolite levels.
In order to define community standards for the minimum information required to describe a protein binder and its target, we have proposed a definition of reporting guidelines as a standard of Minimum Information about a Protein Affinity Reagent (MIAPAR)(2). This is to be implemented by those using and producing affinity reagents and for their application to biobanked samples. Through MIAPAR, required information is structured so as to allow for entry into databases and enable useful querying and automated data analysis. It will be a basis for the accurate and unambiguous description of binders as molecular tools in the resource catalogue and other public databases.
At the initiative of BBMRI WP4 partners, discussions and a joint meeting have taken place with those with similar responsibilities in three other ESFRI infrastructures (ECRIN on clinical research, EATRIS on translational medicine, and ELIXIR on biological information) with the aim to coordinate activities and harmonise practices. A group overseeing this coordination activity has been formed under the leadership of Dr Peter Luijten (EATRIS).

Key questions to be addressed by WP 1.3 include:

Proteins, binding reagents and other molecular tools.

- How can extensive sets of affinity reagents for protein analyses be catalogued and made widely available?
- For what classes of protein products are there - or will there be - reference sets of reagents?
- What measures must be taken to validate and QC such reagents and their application for specific assays on biobanked samples?
- How can the results of analyses be standardised to permit comparison of results obtained in different laboratories?

Methods.

- What methods are currently available to store and to analyse biological material, and what new opportunities can be expected over a shorter and longer perspective?
- Is it possible to standardise and communicate methods and protocols in a manner that can be annotated with any molecular analysis of any biological specimen?
- What information systems and databases can be implemented to ensure efficient development of critical methods, and prompt access for the research community?

Three main tasks are envisaged.

Task 1: To catalogue European resources for affinity binding reagents (mainly antibodies but also other molecular binders)(3). Centres with publicly accessible reagents will be identified and information collected, initially in response to questionnaires. An inventory of reagents will be prepared using the database ontology developed within the ProteomeBinders project (4)(5). A dedicated BBMRI database will allow users to visit one online 'warehouse' and find all available affinity reagents from different providers together with experimental documentation that facilitates easy comparison of cost and quality. The database will include defined specifications for reagent sets and agreed minimum annotations (MIAPAR), as established during the preparatory phase. Data related to performance and quality assurance will be tracked and made generally available, and feedback from users will be annotated. The catalogue will facilitate the identification and retrieval of optimum reagents for research purposes, and enable an assessment of the level of coverage of biomarkers of the relevant diseases (e.g. plasma, cancer) for application in biobanked samples.
Task 2: To catalogue methods and technologies applicable to biobanked samples. The task will be to expand and populate the recently created MolMeth database with validated methods for analysis of nucleic acids, proteins and metabolites, applicable to biobanked samples(6)(7)(8). The database will also include protocols for sampling procedures and storage conditions, together with other resources such as information about materials, contact data and literature references. All protocols will be linked to the relevant parts of the biomolecular resources portal (below). Another part of this task will be the creation of detailed specifications of the inputs and outputs using well defined ontologies. This work will allow MolMeth to suggest steps for the protocol author or, given a start condition and a goal, even produce an entire protocol by combining protocols already stored in the

database. The automatically generated protocols would then require laboratory validation and testing. The computational abilities arising from structured protocol specifications will be crucial in the development of harmonised standards in several pan-European research infrastructures. The database will be improved with stronger ties to standards initiatives to ensure that all protocols are unambiguous and that all steps are described in sufficient detail.

Task 3: To maintain a publicly accessible, common web-based biomolecular resources portal. This will constitute a major centralised information site for European technology resources and platforms serving the major biobanks. As noted, the portal has been under construction (http://www.bbmri-wp4.eu/) and will be available as a test site during the preparatory phase. It will include links and dedicated search engines to extensive inventories of resources including those for DNA, proteins, binders, biomarkers, arrays, cells, databases, genomes, metabolites, standards, etc. It will also provide links to the relevant parts of related infrastructure projects such as EATRIS, ECRIN, ELIXIR and INSTRUCT to reinforce cooperation and harmonization between related interests. A work group will be formed to develop a plan with the aim to automatically and continuously update the content of the portal.

Deliverables

D1.3.1: Database of binding reagents for analysis of biobanked samples and of European resource centres providing relevant services (m36)

D1.3.2: Database of methods for analysis of biobanked samples (m48)

D1.3.3: Web portal for resources and molecular technologies applicable to biobanked samples (m24)

References

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Work package 1.4

Work package number	1.4		**Start date or starting event:** Mo. 1					
Work package title	***Training and dissemination***							
Activity Type	COORD							
Participant number	**8**	**5**	**9**	**15**	**16**	**18**	**19**	**24**
Participant short name	IPRI	INSERM	UniMAN	NIPH	EUR	LSG	UTARTU	IPPOSI
Person-months per participant:	24	12	12	12	12	12	12	6

Objectives

The role, nature and the development of research training is important to fully exploit human resources. Within BBMRI I3 a European Master/PhD curriculum in Management of Biological Resources will be developed that will educate and promote standards applicable to all biomedical biobanks. To ensure that biobanks are developed and used to their full potential, it is essential that researchers and others associated with biobanking have access to the best possible training and career development opportunities at all stages of their professional life. Training is, in itself, a type of dissemination. Another closely linked type of dissemination concerns the needs for exploitation and better dissemination of results. To address these a dissemination plan will be developed and implemented early in the project in close cooperation with all other Work Package leaders .

Description of work

Task 1. European training agenda:
An inventory of the European biobanking training landscape will be made, which also identifies the leading universities and training sites in the field. In connection to the inventory and in collaboration with course providers and similar initiatives that develop biobanking training (e.g. P3G), this WP will identify possible topics for Joint Seminars, Summer schools, short term/long term fellowships and transnational supervision of PhD theses in the field of biobanking research. These activities and inventories will help to build a future European training agenda in biobanking. It is intended to start with the first European Master and/or PhD programmes during the lifetime of the project.
Task 2. Dissemination and public relations:
In addition to scientific publications and publications of the project partners and the international conference, this WP will generate flyers and brochures for experts and lay public to inform about the importance of BBMRI for Europe . Furthermore, a website will be set up for internal as well as external communication. The content of the documents will be prepared in close collaboration with the work package leaders. Dissemination of biobanking research outputs (actual and methodological) to the non-specialist audience will be coordinated through the BBMRI Stakeholders Forum Patient Working Group.

Deliverables

D1.4.1: European biobanking training agenda (mo 24)

D1.4.2: Project website (mo 6)

D1.4.3: Three international biobanking training courses (mo 18, 30,42)

D1.4.3: Patient Organization Training Workshop (mo 18)

D1.4.5: PR material (mo 12-48)

Work package 1.5

Work package number	1.5	Start date or starting event:			Mo. 1		
Work package title	*Strategic health programme coordination*						
Activity Type	COORD						
Participant number	2	4	8	10	24		
Participant short name	MedUG	UTU	IPRI	ULEIC	IPPOSI		
Person-months per participant:	24	12	4	4	12		

Objectives

The DIAL-BBMRI proposal builds on the work done within the BBMRI preparatory phase (PP) and will deliver key tools for the implementation of BBMRI under the ERIC legal entity (BBMRI-ERIC) and serves as a proof-of-concept for accessing BBMRI resources and services. Because of this intimate relationship a good coordination of both projects (DIAL-BBMRI and BBMRI-PP) is essential. Furthermore, BBMRI-PP has important synergies with other biological and medical sciences (BMS) research infrastructures of the ESFRI road map and takes care of the biobanking-related issues for all other BMS infrastructures. Furthermore, BBMRI-PP coordinates a joint communication task force and prepares a joint white paper to be presented to the European Parliament in 2010. These synergies should be considered in procedures established within DIAL-BBMRI. Rules and procedures of BBMRI-PP build on the OECD best practice guidelines for biological resource centres, which define key issues for transnational access, quality assurance, safety and security. This provides also a common basis for transnational sample and data access from/for resource centres in OECD Member or partner states outside of Europe and establishing efficient global collaboration. Compatibility with global initiatives is also facilitated by the fact that BBMRI-PP recommends the WHO/IARC guidelines for biological resource centres as templates for internationally harmonized SOPs. To optimally coordinate activities between the different global biobanking initiatives and avoid gaps or work duplication, this horizontal cross-biobank coordination has been structured as a specific work package per se WP1.6 (see below). Finally DIAL-BBMRI has to coordinate its activities with the Innovative Medicines Initiative, which represents a major user community from academia and industry requiring access to biological samples and data for biomarker research and development.

Description of work

Task 1: Coordination with BBMRI-PP and BBMRI-ERIC: It is expected that the BBMRI-PP leads to the implementation of BBMRI-ERIC at the end of 2010. To guarantee complementarities and avoidance of duplication, the activities of DIAL-BBMRI have to build on previous achievements and consider the specifications as defined within BBMRI-ERIC. To facilitate this, the coordinator of BBMRI-PP will be in charge of this strategic integration work package. Regular (at least two per year) joint Steering Committee meetings of BBMRI-PP/BBMRI-ERIC and DIAL-BBMRI should streamline all activities. All reports and meeting minutes will be made mutually available. The web sites will cross-reference the relationship of these projects and explain the synergism and complementarities. DIAL-BBMRI will participate in events that might emerge from the BBMRI-PP white paper. The BBMRI-PP Stakeholder Forum will expand its work also into DIAL-BBMRI. A joint stakeholder/user conference will be organized in 2011.

Task 2: Coordination with OECD and WHO/IARC biological resource centre activities: All technologies developed and procedures established for providing efficient access within DIAL-BBMRI should also be suited for global research collaborations whenever feasible. This should be facilitated by implementation of the OECD best practice guidelines for biological resource centres and the WHO/IARC guidelines for biological resource centres as a basis for the DIAL-BBMRI. The implementation of these guidelines in DIAL-BBMRI will be compared with the implementation in biological resource centres outside of Europe. A series of small workshops with non-European biological resource centres should demonstrate and further enhance the global compatibility of DIAL-BBMRI standards, and wherever possible export access procedures.

Task 3: Coordination with the Innovative Medicines Initiative (IMI): DIAL-BBMRI will organize a joint workshop with IMI–EFPIA representatives as well as coordinators of IMI-projects that have a major biobanking or biomarker focus in order to define access needs and emerging FDA and EMEA standards for biological materials used for biomarker development. Eventually DIAL-BBMRI participants will also apply to upcoming IMI calls to establish a practical relationship between these two programmes.

Deliverables

D 1.5.1: Cross reference in web sites (mo 3)

D 1.5.2: Joint stakeholder/user conference (mo 14,32)

D 1.5.3: Joint Steering Committee meetings (mo 36)

D 1.5.4: Workshop with non-European biological resource centres (mo 24)

D 1.5.5: Workshop with IMI-EFPIA representatives and IMI-coordinators (mo 20)

Work package 1.6

Work package number	1.6	Start date or starting event:					Mo. 1	
Work package title	*Global biobanking coordination*							
Activity Type	COORD							
Participant number	15	2	6	7	10	12	25	27
Participant short name	NIPH	NTNU	WTSI	THL	ULEIC	HMGU	HeLEX	P3G
Person-months per participant:	12	4	4	4	4	4	4	8

Objectives

This WP builds upon a number of initiatives working to build a cost-effective and harmonized network of biobanks across Europe (and beyond) for the purpose of unravelling complex disease aetiology and translating findings into new therapies, diagnostics and methods of prevention. Recognizing that the magnitude and scope of this agenda clearly transcends the reach of individual initiatives the EU has invested significantly in a range of projects to tackle various components of this work. This includes research projects (e.g. GenomEUtwin, ENGAGE), infrastructure building (e.g. BBMRI), the development of tools and technologies (e.g. GEN2PHEN, MOLPAGE) and coordination actions (e.g. PHOEBE); all contributing fundamental, but distinct work towards the ultimate goal of biobank interoperability. While there is still much to be done, significant inroads have been made. Collectively, such projects have provided the larger community with early versions and the first refinements of standards, norms, tools, technologies, compatible bioinformatics, catalogued information and consensus documents to facilitate the design and management of biobanks and to promote the exchange, management and analysis of data and biospecimens. Much of this work is relevant to population-based and clinical biobanks, and most of the work has been developed in tandem with relevant ELSI components.

Many of these harmonization outputs are already being brought forward through their integration into new projects and biobanking activities and will pave the way for us to mobilize better data more fully, using cutting edge methodologies and informatics. To achieve this we recognize that it is critical that we coordinate our resources across the EU to maximize our scientific and monetary investments, avoid duplication of effort and accelerate the science most efficiently. Such cross-biobank strategic coordination was emphasized in the November 2008 Brussels meeting of 25 EU funded biobanking projects (1) and reiterated in the March 2009 international conference *'Harmonizing Biobank Research: Maximizing Value-Maximizing Use'(2)* . Building upon our experiences in the FP6 Coordination Action, PHOEBE (3) which recently ended, this WP will help to realize these ideas by building inter-project biobank coordination into the DIAL-BBMRI. The goal of this WP, to conduct inter-project, operational biobank coordination, is congruent with the goal of similar WPs in related initiatives such as BioSHaRE and P3G. Through interaction and strategic coordination with our sister projects we will be able to efficiently pull together the requisite expertise and experience from our projects and identify challenges and critical issues, exchange ideas, and develop innovative paths forward. This strategy will avoid duplication of effort and will mutually benefit the work across projects through real-time communication and coordination.

Description of work

The work conducted in this WP will encompass two major tasks.

Task 1. Strategic scanning across the biobank landscape, including scientific scanning and societal scanning so that we can develop a coordinated strategy for responding to the evolving science and needs. Interfacing with other projects and activities is critical to accomplish both of these tasks. This will also provide a forum for identifying challenges and articulating next steps forward that can then be brought back to the relevant projects to maintain synergy in our work. Such interactions will also promote information transfer and dissemination of DIAL-BBMRI outputs into the larger community.

The program of strategic coordination and scanning will be coordinated by JH and co-led by the other members of the WP (PB, KV, EW, MP and JK) whose collective expertise and respective networks spans areas critical for carrying out the WP work proposed herein. We will also interact closely with the other WPs in DIAL-BBMRI so that we can identify areas where strategic coordination between projects is essential and provide information,

where relevant, to activities overseen in the BBMRI-IC WP focused on the strategic integration of infrastructural aspects of DIAL-BBMRI with other public/private health-related activities.

Task 2. Integration, coordination and communication of DIAL-BBMRI operational biobanking activities with those in ongoing related initiatives. This is essential to ensure complementarity and coordinated evolution of major project outputs.

Interface activities between DIAL-BBMRI and external projects will be mediated via regular (monthly) teleconferences of the WP, by face-to-face meetings occurring at least twice a year and where possible linked to other meetings, and through the WP teams engagement in related initiatives. In between meetings, the group will maintain close informal links and encouraged to speak regularly by phone and to interact frequently via email. The members of this WP are highly networked in leading prominent activities that are shaping the biobanking landscape and will be continually interfacing with these various activities and feeding information back to the WP as part of our scanning activities.

Deliverables

D1.6.1 Identify key initiatives to interface with (mo 3)

D1.6.2 Develop a strategic integration plan for systematic and regular inter-project communication (mo 6)

D1.6.3 Develop a strategic horizon scanning plan for the science and the societal issues (mo 12)

D1.6.4. Meet every 6 months with relevant projects and produce an overview report of the key coordination and scanning aspects (mo 6-48)

References

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Work package 1.7

Work package number	1.7	**Start date or starting event:**		Mo. 1
Work package title	***Wiki-based legal repository***			
Activity Type	COORD			
Participant number	**14**	**5**		
Participant short name	LP	INSERM		
Person-months per participant:	12	5		

Objectives

The mission of the WIKI Legal Platform is to properly embed the pan-European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) into the European legal framework, by providing the BBMRI community with immediate access to quality-controlled legal templates. To that end, the platform is designed as an operational tool that allows online, 24/7, uploads, updates, upgrades, retrieval and downloads of state of the art legal documents (national and international) that are necessary to ensure that the cross border research activities envisaged under BBMRI are legally compliant. The templates address all ELSI issues pertinent to the activities of the BBMRI community, including but not limited to consent, data protection, access policies, feedback, tissue transfers, data transfers, IP and benefit sharing. The platform aims to cover all European jurisdictions present in BBMRI. In order to sustain the currency, accuracy and comprehensiveness of the legal templates, the platform will develop a network of qualified lawyers (academic or professional), from each jurisdiction represented in BBMRI (National Correspondents), who will monitor, review, assess, and discuss the uploads, updates and upgrades of the legal documents. Collectively, the envisaged network of National Correspondents could develop integrated pan-European legal helpdesks for the BBMRI Community, in collaboration with compatible initiatives and platforms currently contemplated by projects such as PHGEN and GEN2PHEN. Finally, as the WIKI Platform also provides ample opportunity for discussion and is open source, we will explore its potential to serve as a bottom up, Web 2.0 governance mechanism, in close collaboration with the BBMRI Stakeholder Forum and related projects such as the PATIENT-PARTNER (FP7).

Description of work

Task 1: Recruitment of National Correspondents from each BBMRI jurisdiction.

Task 2: Training of National Correspondents.

Task 3: Mobilizing BBMRI community as contributors to the Platform

Task 4: Population of National Legal Templates.

Task 5: Population of cross European Legal Templates.

Task 6: Moderation of WIKI contributions to the platform.

Task 7: Alignment of Platform activities with other BBMRI-WorkPackages and the BBMRI Stakeholder Forum.

Task 8: Maintenance of the platform (updating, upgrading, QA and QC of contents and user interface.

Deliverables

D.1.7.1: National Templates first version public (mo2)

D.1.7.2: European Cross Border Templates first version public (mo 6)

D.1.7.3: Updates and upgrades of legal documents (mo 2-48)

D1.7.4: Full version of Wiki Legal Platform (mo 12)

D1.7.5: Final version of Wiki Legal Platform (mo 48)

Work package 1.8

Work package number	1.8	Start date or starting event:		Mo. 1	
Work package title	*Quality management*				
Activity Type	COORD				
Participant number	9	3	5	11	
Participant short name	UniMan	NTNU	INSERM	KI	
Person-months per participant:	12	4	4	4	

Objectives

Quality assurance is fundamental to the successful operation of any biospecimen repository. The use of standardized protocols for collection, storage, processing, and distribution of specimens, and the use of common data elements for the annotation of specimens at each of the individual network participant locations make comparative research across participating institutions possible. To ensure that the collection, processing, annotation, storage, and distribution of biospecimens occur at a consistently high level of quality, it is necessary to have a multi-tiered, fully integrated quality assurance system and standard operating procedures. Quality assurance starts with the training of personnel before biospecimens are ever collected and includes everything up through considering researcher feedback on sample quality. In the preparatory phase of BBMRI, we have developed in coordination with P3G biobank guidelines integrating items from several existing ones : OECD, ISBER, IARC and the French norm for biobanks (NFS96900) (www.p3gobservatory.org). Furthermore, several biobanks in Europe were certified on the basis of either ISO 9001 or the French norm NF S 96900 (AFNOR). For example in UK 3 on the basis of ISO 9001, France 10 on the basis of NFS96900, Germany …based on these outcomes and experience DIAL-BBMRI will:

- Develop, harmonize and implement best practices for collection, processing, annotation, storage, and distribution protocols to ensure the highest quality samples and comparability of research results.
- Develop and implement appropriate QC testing on each specimen, such as histopathology (H&E), immunohistochemistry, testing for DNA/RNA integrity, tissue quality and other QC testing as appropriate.
- Train collection personnel and supply them with standard protocols to follow in order to provide comparable specimens for research purposes.
- Advice and train personnel to implement Quality Assurance procedures in biobanks
- Foster researcher feedback about sample quality to re-examine quality control procedures

Description of work

Task 1. In coordination with WP 3.1 and 3.2 develop, harmonize and implement best practices for collection, processing, annotation, storage, and distribution protocols to ensure the highest quality samples and comparability of research results. This includes harmonizing standards for storage depending on tissue type and preservation condition use common data elements for the annotation of specimens at individual network participant locations in order to make comparative research across participating institutions possible.

Task 2. Develop and implement appropriate QC testing on each specimen, such as histopatholgy (H&E), immunohistochemistry, testing for DNA/RNA integrity, tissue quality and seek developing new QC testing procedures where required.

Task 3. Set up training seminars and summer schools to train biobank personnel, including pathologists, to harmonize and implement SOP and quality assurance in their centres.

Deliverables

D1.8.1: Workshop with biobank personnel and report on best practices (mo 18)

D1.8.2: Workshop with biobank personnel and report on quality control of resources (mo 24)

D1.8.3: Seminar or summer school on quality assurance (mo 12)

References

http://www.p3gobservatory.org/repository/guidelines.htm

AFNOR:
http://www.boutique.afnor.org/NEL5DetailNormeEnLigne.aspx?&nivCtx=NELZNELZ1A10A101A107&ts=8888803&CLE_ART=FA156209

Work package 1.9

Work package number	1.9	Start date or starting event:		Mo. 1			
Work package title	*Access and cost management*						
Activity Type	COORD						
Participant number	5	3	12	13			
Participant short name	INSERM	NTNU	HMGU	BBT			
Person-months per participant:	12	4	4	4			

Objectives

BBMRI-I3 project takes European collection of biological resources to new heights of coordination and efficiency providing new services and better access for users. WP 1.9 will provide a one-stop access to the collections of the European biobanking community, expertise and services via a searchable web portal building on the outcome of BBMRI project preparatory phase.

It will build on these outcomes to foster access to other parties (including from private sector) by providing :

- Free access to documents, SOP and best practices developed by BBMRI-I3,
- Open access to published results and data published in coordination with partners of BBMRI-I3. The Open access will be based on the Berlin declaration (open access-2003)
- Fair access to samples and related clinical data. Fair access is primarily based on merit review of the proposal by the scientific and ethical committee with the help of external experts. This review will be based on a number of principles shared with the review procedure of projects used in FP7 (rules for submission, cordis). These include :
    - **Excellence.** Projects selected for funding must demonstrate a high scientific quality.
    - **Transparency**. Funding decisions must be based on clearly described rules and procedures, and applicants should receive adequate feedback on the outcome of the evaluation of their proposals.
    - **Fairness and impartiality.** All proposals submitted to BBMTI-I3 for access to samples are treated equally. They are evaluated impartially on their merits, irrespective of their origin or the identity of the applicants.
    - **Confidentiality.** All proposals and related data, knowledge and documents communicated to the scientific committee are treated in confidence9.
    - **Efficiency and speed.** Evaluation, award and grant preparation should be as rapid as possible commensurate with maintaining the quality of the evaluation
    - **Ethical and legal considerations:** Any proposal which contravenes fundamental ethical principles or which fails to comply with the relevant legal procedures may be excluded at any time from the process of evaluation, selection and award..

To achieve this aim WP 1.9, in close collaboration with WP 3.1 and WP 3.2, will:

- Develop a procedure to review and prioritize requests to samples and associated data
- Study the possibilities to encourage biobanks to keep an adequate supply of specimens to keep up with customer/researcher demand.
- Develop SOP, best practices and appropriate tools to increase support for the resource and investment in the quality of the resources collected and their associated data. Free access will be offered for these documents and tools.
- Harmonize cost assessment to resources, associated data and access to services and expertise.
- Implement appropriate methodology and indicators to assess the accrual of distribution to public and private partners and the impact of BBMRI-I3 on socioeconomic issues.
- Encourage researchers accessing to samples and data through BBMRI-I3 to publish their work according to Open Access paradigm.

Improved data and greater access to a wider range and better maintained resources as proposed by BBMRI-I3 will provide European academic and industrial with a huge advantage over the rest of the world and a road to delivering the bioeconomy.

Description of work

Task 1 : In coordination between WP 3.1 and 3.2, develop and harmonize existing procedures of access to meet a common set of criteria as reviewed by the scientific and ethical committee with the help of external experts. These criteria include: Scientific merit, study design, technical parameters (e.g., reproducibility, sensitivity, specificity, throughput, automation, and cost), clinical or scientific impact, practicality and feasibility (e.g., amount of tissue, and number of samples required), and collaborative strength. The procedure will be made available on the web site

Task 2. Coordinate with WP 2.6 and 1.9 the development of an access procedure to expertise, facilities and tools in the legal and ethical field. The procedure will be made available on the web site.

Task 3. Determine and harmonize the actual costs of collecting, processing, storing, and distributing tissue samples combined with the amount of clinical information and the level of annotation associated with the sample. These will be different for resources from different origins/ tumors, blood, brain…This will be coordinated with Public Population Project in Genomics (P3G). The aim is to develop a common operating practice on a cost recovery basis (at least for the government and non-profit organizations) to financially sustain the biobank. For the sake of information, an estimated cost for access for resources from tumor or blood is given in annex YY

Task 4. Implement appropriate evaluation procedures and indicators to assess a) the percentage of distribution of samples and data to private and public partners and b) the impact of BBMRI-I3 on socio-economic issues.

Deliverables

D 1.9.1: Joint stakeholder/user conference and publication of procedure on web site (mo 14, 32)

D 1.9.3: Workshop with non-European biological resources centres (mo 18) and report on access costs (mo 20)

D 1.9.4: Report on accrual of distribution and socio-economic indicators (mo 24)

References

Open access-2003 :http://oa.mpg.de/openaccess-berlin/berlindeclaration.html

Rules for submission of proposals and and the related evaluation, selection and award procedures (posted on CORDIS)

Work package 2.1

Work package number	2.1	Start date or starting event:		Mo. 1			
Work package title	***Biobank Informatics***						
Activity Type	RTD						
Participant number	**11**	**1**	**2**	**7**	**10**	**17**	**21**	**26**
Participant short name	KI	LUMC	MedUG	THL	ULEIC	deCODE	TUM	UniKlu
Person-months per participant:	96	72	24	24	12	12	48	48

Objectives

Key components of BBMRI are comprehensive collections of biological samples from different (sub-) populations in Europe, which should be linked with continuously updated data on the health status, lifestyle and environmental exposure of the sample donors. This interlinking can only be achieved in a federated network of centres established in most, if not all, European Member States [Litton et al., 2007]. Therefore, the format of BBMRI should be a distributed hub structure in which the hubs coordinate activities, including collection, exchange and analysis of samples and data for the major domains. The IT-infrastructure, which employs federated database technology, will federate the complex network of hubs, members and partners into a single virtual infrastructure. The deliverables of WP2.1 will provide the requirements and the groundwork for schemas for a federated database system that enables searching for interesting and comparable material across European Biobanks. Special emphasis is given to confidentiality, privacy and the adherence to special ethical procedures put in place by the participating biobanks. Furthermore, 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, including user interfaces. Given the budgetary restrictions of the I3 call, a full-fledged interconnection of all participating biobanks in BBMRI-PP is out of reach. The intention is to concentrate on developing and implementing the core features for the IT infrastructure for a subset of leading European biobanks, while national funding for Biobank initiatives will be mobilised and used for interconnection of the growing set of collections.

Description of work (possibly broken down into tasks), and role of participants

BBMRI WP 2.1 "Biobank Informatics" can be further split into three major activities. Prof. Jan-Eric Litton will be overall responsible for the Biobank informatics activity. Prof. Johann Eder and Prof. Klaus Kuhn will have the main responsible for subactivity 2.1.2, while subactivity 2.1.3 will be managed by Dr. Barend Mons.

Subactivity 2.1.1: "Coordination of biobank informatics and internal/external collaboration"

This includes coordination of the two remaining activities 2.1.2 and 2.1.3, and will also act as the interface towards other activities within the BBMRI project and external collaboration with other projects connected to the domain of biobank informatics. Coordination for biobank informatics will be required on three levels; (1) coordination within WP 2.1 itself (i.e., internal coordination for the activity), (2) coordination with the other activities of the BBMRI project (i.e., external coordination for WP 2.1 or internal coordination for the BBMRI project) and (3) coordination with activities related to WP 2.1 in other biobanking/health infrastructure initiatives (i.e., external coordination for the BBMRI). During the BBMRI PP, the informatics work package (WP5) has in close collaboration with the ethics work package (WP6), been working towards a BBMRI Data Protection Standard, compliant with the EU Data Protection Directive, to govern cross-border DP issues. Efforts have consisted of describing realistic scenarios which have been further analyzed from a data protection point of view. However, several classes of these scenarios exist, and some type of data may be less sensitive than other, requiring a continued collaboration on DP issues within BBMRI. Therefore close coordination of future activities in WP 2.1, 2.3 and 3.3 is necessary. External coordination for the BBMRI. Underpinning the desire to interact with related domains is based on the belief that especially at the intersections of the disciplines significant scientific progress will be realized in the coming years. Facilitating interaction between the various fields, therefore, is an important objective of BBMRI. This is an area with close interactions with WP1.6.
The following tasks are proposed for subactivity 2.1.1:

Task 1: IT coordination of implementation tools and technology for biobanking
Task 2: Collaboration with WP 2.3 and WP3.3 for a Data protection policy for BBMRI
Task 3: Work together with ELIXIR to define common grounds. Furthermore, collaborate closely with other biobanking/health infrastructure initiatives (such as IMI, epSOS and HEALTH.2010.1.1-1:, Gen2Phen EU-project and the DataShaper project to reach interoperability of biobanks, both at the concept- and at the sample character (comparability) level.

Subactivity 2.1.2 "Continuation of requirement analyses, development, and implementation of a European system integrating biobank information"

Subactivity 2.1.2 is essentially a direct continuation of BBMRI PP WP5 activities, which can be summarized as:
1: Consensus achievement on a general information management system and inventory of standard-related issues.
2: Explore systems for maintaining unique and secure identities (object models) for specimens, subjects and biobanks.
3: Explore a complete strategy for communication between biobanks including a common nomenclature, compatible software techniques and appropriate information transmission policies

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. The "proof-of-concept" is set up to analyze the adequacy and consistency of the requirements, and to show the feasibility of a federated architecture. Its interfaces are not hardened for general deployment and its internal structure is not optimized.
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 terminology mapping service can directly benefit from a knowledge base as resulting from activity 2.1.3.
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.
The following tasks, occasionally interrelated, are proposed for subactivity 2.1.2:
Task 4: Integration of several European biobank IT applications into the BBMRI PP integration prototype to enable testing and evaluation in a large-scale biobank network.
Task 5: Extended requirements analysis for different user groups for the use case classes defined in BBMRI PP including a formal consensus study (e.g., a Delphi study) to analyze key parameters (data content and volume, frequency of queries, numbers of users, etc.) for the biobank federation.
Task 6a:. Refinement of design and implementation of a service architecture considering the pre-specified requirements along with further elaboration for the hub and spokes topology. This includes national hubs that have been created during the BBMRI PP phase
Task 6b: Elaboration and integration of the existing services from the BBMRI PP portal system and the BBMRI integration prototype into the service architecture. Specification of service interfaces and functionality for additional services for connection, registration, schema integration, terminology mapping, integration, caching and indexing. Optimization of data structures and access methods.
Task 7: Refinement and elaboration of the federated schema.
Task 8a: Setup of a service infrastructure with the services from the BBMRI PP portal system and the BBMRI PP prototype. Development of the additional services from the design description of the service architecture also covering technical infrastructure requirements. This will comprise the connection between the BBMRI PP portal system and the integration service, between the integration service and the service interface from the BBMRI PP integration prototype. It will also include a connection between the terminology mapping service resulting from subactivity 2.1.3.
Task 8b: Development of a biobank connection toolkit to support the integration of component systems;
Task 8c: Further development of the BBMRI PP portal system including exploration, development and evaluation for efficient interfaces for researchers to access and explore the integrated data.

Task 9: Training and support for users from European Biobanks to implement biobank connection services using the biobank connection toolkit.

Subactivity 2.1.3 "Development of an online multilingual biobank terminology system and management, breaking the language barrier between descriptions of cross-European biobanks, including user interfaces"

This will be partly new work and partly an extension of the previous work related to the Biobank Lexicon, which in turn is related to the linguistic- and ontology task of the BBMRI PP WP5.
Interoperability of Biobanks is crucial as many individual collections are too small to serve the perceived research needs, both of academia and industry. Interoperability can be defined at minimally two levels:
1. The harmonization of the protocols for data collection and description in general.
This is the focus of WP1.2 and the P3G/BBMRI Datashaper collaboration, and will therefore not be addressed here. For this purpose we will collaborate closely with the Datashaper team.
2. Metadata being captured or expressed in the same format (the core business of this WP)
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. However, these terms introduce a range of ambiguity problems and thus destroy interoperability. In order to make these tags, which define the scope and content of individual samples and their collections interoperable, the metadata need to be harmonized, removing jargon and language based ambiguities.
The first step in this interoperability process is the use of a well-mapped and open terminology system. A terminology system usually maps terms to a 'numerical' identifier and defines the meaning of the term. The Open Terminology System Used for this purpose is the Concept Wiki[1], currently maintained by the Netherlands Bioinformatics Center (NBIC) and Leiden University Medical Center (LUMC). Additional (language or domain specific) terminology systems can be mapped to the 'also referred to as' (ARTA) table in the Concept Wiki environment (see definition of biobanking) and as soon as the term or the identifier is present in the 'Also Referred to As' collection, the term/identifier is interoperable.
The second step is to recognize terms and identifiers (tokens) in free text fields as referring to a defined concept. Using state of the art concept taggers synonyms can be resolved by disambiguation and mapping for which most basic research work has been completed, to a large extent by our group [Schijvenaars et al, 2005, Schuemie et al, 2007, Altman RB et al 2008,] and the first tools are reaching industrial grade status.
For the following community languages, the Medical Subject Headings of the National Library of Medicine (also used for tagging PubMed abstracts) have already been translated: German, Portuguese, Spanish, French, Russian, Romanian, Polish, Greek, Dutch, Turkish, Swedish and Italian. Also other languages, such as Japanese, Arabic, Thai, Chinese, and Bahasa are covered. These MeSH terminologies can be mapped in a straightforward way to the Concept Wiki. The National Medlar centres, who maintain these language-specific versions in collaboration with the USA National Library of Medicine, will be actively engaged in this process wherever possible. Many terms not well covered in MeSH, such as Gene and Protein symbols, Chemical names and personal names are relatively uniformly used across languages, but will also be translated where needed.
The following activities are proposed for subactivity 2.1.3:
Task 10: Enrich the Concept Wiki with translations as well as with additional terminology systems specific to BBMRI biobanks, including the multi-lingual lexicons already developed in BBMRI PP.
Task 11: Develop user-friendly interfaces in multiple languages to turn free text or term-based tags into concept tags that are unambiguous, computer interpretable and therefore fully interoperable.
Task 12: Provide multi-lingual tagging systems as web services to a growing number of languages and BBMRI partners on a close to 24/7 basis to tag their text input on an individual as well as a batch wise basis. (in case this is becoming a widely used service, it will need to be set up as a small-fee based professional service). For some languages, Open Source Stemmers may need to be tested and implemented to improve concept recognition in that language.
Task 13: Provide semantic-web enabled search, mapping and analysis tools to reason over biobank collections' and present easy to navigate biobank maps in Google maps based on concept-similarity (smoking=rauchen=roken=fumer) . Concept indexing can be installed on local biobank hubs if so desired and training will be given, in close interaction with WP 1.4 to biobank information managers to ensure that meta data are increasingly captured in a fashion that enables optimal interoperability. Similarly, workshops on semantic web based distributed data handling and storage will be organised in a co-ordinated fashion with the other elements

[1] www.conceptwiki.org

of this workpackage, and under the auspices of WP1.4.

Deliverables (brief description and month of delivery)

D2.1.1: Biobank informatics activity-specific project plan (mo 3)

D2.1.2: Joint report on Data Protection with activities 2.3 and 3.3 (mo 36)

D2.1.3: Roadmap and reports for project collaborations (mo 12, mo 60)

D2.1.4: Test report of integrating IT applications into the BBMRI PP prototype (mo 6)

D2.1.5: Extended requirements specification, comprising the results of the consensus process for the core and the extended data sets (mo 12)

D2.1.6: Test of implemented services, improvement of service implementations, and refinement of the service architecture, with specific regard to security and test of the biobank toolkit (mo 24)

D2.1.7: Refinement of the federated schema (mo 18)

D2.1.8: Results of impending terminology mapping services in relation to Subactivity 2.1.3 D2.1.9: Roll-out after preparation of online user-guide (describing installation and operation of client software) (mo 48)
D2.1.9: Preparation of online user-guide (describing installation and operation of client software), roll-out (mo 48)

D2.1.10: ConceptWiki Biobank version (mo 6)

D2.1.11: Design, description and implementation of the user interface (mo 9)

D2.1.12: Design, description and implementation of an interactive tagging system (mo 18)

D2.1.13: Design, description and implementation of analysis tools (mo 36-24)

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Schuemie MJ, Kors JA, Mons B, Journal of Computational Biology 2005 Jun, 12:554-65

Work package 2.2

Work package number	2.2	Start date or starting event:	Mo. 1				
Work package title	***Biobanking technology and logistics***						
Activity Type	RTD						
Participant number	**3**	**9**	**11**				
Participant short name	NTNU	UniMan	KI				
Person-months per participant:	24	6	6				

Objectives

Europe needs a competitive biobanking infrastructure in terms of the physical sample-handling and storage solution, logistic processes and IT systems. The international research focus of today is on creating national large population and diseased based sample collections, with several hundreds of thousand participants each, potentially totaling many millions of participants all across Europe. The reason for large scale collections is that large studies yield sufficient statistical power in connecting genetics, environment and subsequent outcome of disease. Since each participant normally generates 10-100 samples stored, this requires processing and storing of many millions of samples in each cohort collection. The creation of large scale national collections has begun in a few member countries and is in the planning phase in many others. The requirements to process, store and withdraw samples from large collections, urges an evidence-based upgrade of the European biobanking infrastructure.

The problems with the current biobanking infrastructure are several. The infrastructure is operated by local biobanks all over Europe; with little or no harmonization in standards, format and level of sample-handling quality. Most local biobanks are manual or semi-automatic, which limits them to small studies and small or no withdrawals. Especially withdrawal of samples is today very cumbersome. This means that previous efforts to collect and store samples, commonly fail since the possibility to use the samples is limited. The current biobanking infrastructure is expensive to run due to the small scale and there is a large variation in quality and operational safety, which raises a barrier for joint studies since conformity in quality of the collections can't be assured.

In BBMRI-PP, biobank technologies and research on the infrastructure have not been specifically addressed. In BBMRI-I3, this will have a much stronger focus in order to support and facilitate transnational access of samples and/or prepare for requested analysis.

The solution we propose is a large-scale, cost-efficient automatized and streamlined biobanking infrastructure. Converting to automatized and streamlined processes, in conjunction with volume purchase power of consumables, will drive down the cost for biobanking service by a factor 3-5. Automated solutions are typically very costly, but often necessary to both support the need for high through-put activity and improved quality in sample handling.

De novo collections of biological material are more readily supported by automated technologies where the best possible infrastructure and tailor made logistics will be easier to implement to fit the purpose. Such solutions are technically available throughout the whole sample handling process. A main challenge will in many cases be the costs involved, especially for automated storage solutions at temperatures below – 80°C.

Older collections may also be transformed into automated sample handling procedures, but with greater challenges involved in standardizing formats.

So far, few initiatives have been taken between biobanks to seek a collaborative approach to these challenges. The costs involved and the technical complexity calls for common and joint efforts, preferably in collaboration with the industry. These solutions will also be more cost effective if they are directed at more larger-scale, regional or national biobank establishments. Possible customer/industrial collaboration must be in full compliance with existing EU-requirements for purchase and tender procedures.

A few EU countries have recently done bold projects into automatizing parts of their biobanking infrastructure, which has resulted in invaluable insights on how to optimize the path going forward. Already several member states have allocated considerable resources, typically tens of MEUR each, to be used for upgrading the technology and logistics of their biobanking infrastructure. Major initiatives included the national biobanking facility of Norway, the UK Biobank and the national biobanking facility of Sweden (BBMRI.SE). Across Europe, the imminent investment phase in upgrading the biobanking infrastructure to the automatic level is likely to cost hundreds of MEUR.

It is of vital role that the EU BBMRI takes a facilitating role in the imminent automatization phase of the European biobanking infrastructure, to ensure investments are spent in an optimal way. By building on

collaboration, joint standards and joint research towards an evidence-based optimization of biobanking technology we will arrive at our **strategic goal: a unified, high-throughput and cost-efficient European platform for sample-handling and storage.** Driving a unified European sample-handling platform will naturally facilitate unification in other biobanking areas such as data harmonization. A proper development of the physical biobanking infrastructure will make this infrastructure as important for life-science as the CERN infrastructure is for science in physics.

The BBMRI approach to facilitate the best possible outcome of the next generation biobanking infrastructure in terms of physical storage and logistic processes, consists of several parts.

Description of work (Participants)

Task 1.Exploring existing and desired technological solutions. In collaboration with WP 3.1 and WP 3.2, systematically assemble knowledge on existing and planned technical solutions for both population based and clinical biobanks, in terms of e.g. handling logistics, automation and storage (freezer) technology. Apart from systematic literature searches, inquires will be made to participants in BBMRI and other international biobanking networks, such as P3G. The data will be compared to the demands and the most cost-effective and functional technological and logistics solutions for a regional/national biobanking facility will be explored. (All)

Task 2 Explore the diversity and specific requirements related to older biobank collections in order to find the best possible and acceptable protocols for sample handling and access without compromising the establishment of common EU quality standards. Data capture will be as for Task 1. Possibilities for re-formatting older sample collections into modern automated formats will in particular be explored. **(**All

Task 3. Explore sample handling and access procedures. In collaboration with WP 3.1, WP 3.2 and WP 2.1, data will be captured as described in Task 1. The data will be evaluated with the aim to describe an as complete and optimal sample access procedure as possible. The emphasis will be on web- based access, sample handling logistics and automation. (All)

Task 4. Strategic development studies on biobanking technology. Development pilot studies will be launched to explore the feasibility and cost of the most interesting solutions identified in Task 1-3 above. Pilot projects are important to explore the optimal development path and to minimize the technological risk before larger investments are done. These development projects will naturally involve the European high-tech industry and will be essential for them to sustain an innovative competitive advantage. (All)

Task 5. Uniform markers of sample quality. Research on biobanking technology is hampered by a lack of widely acceptable standards for assessing the quality of the sample, resulting in that methods of handling are used as a proxy of quality (e.g. "fresh-frozen within x minutes" et c). We will systematically assemble data (from literature and from the biobanking networks) on methods and markers that are used to assess the quality of samples, for each commonly measured analytes (DNA, RNA, protein, metabolomics et c). The methods for quality assurance will be reviewed in collaboration with the experts in high throughput analysis platforms in the Molecular Resource Infrastructure. It is not likely that actual pilot studies can be conducted within the scope and budget of this I3, but they will be planned and initiated to later serve as a proof of concept for technologies chosen in relation to task 4 and 6. **(**All)

Task 6. Strategic joint research projects on biobanking per se. The development in biobanking is today hampered because there is little research done on the limits of sample-handling logistics. For instance: it is not known how much better sample quality you get by a 30 minute "from needle to freezer" protocol compared to a 30 hours "from needle to freezer" protocol; it is not known how long time the sample quality will stay good in -80 degrees compared to -190 degrees; it is not known if the quality of the sample deteriorates if you repeatedly cycle the sample between -190 and -20 (automatic sample withdrawal robotics works at -20, they cannot work at lower temperatures). This lack of knowledge forces biobanks of today to take the safest route, which implies much more expensive equipment and logistics. Therefore strategic research on biobanking per se will be much welcomed in deciding the optimal solution for the next generation biobanking infrastructure. This knowledge will make it possible to, on a sound evidence basis, set best practice recommendations on

biobanking technology. The most interesting logistic and technological solutions identified in Tasks 1-4 will be evaluated in systematic research projects, where the outcome is the quality of the samples – as assessed using the biomarkers of quality that are identified in Task 5. **(**All)

Task 7. Dissemination of knowledge. When the member states make their decisions on investing in the next generation biobanking infrastructure, the EU BBMRI can ensure that they are well informed on the various options in biobanking technology. Results of the work in Tasks 1-6 will be published in the MedLine-indexed scientific literature. In addition, we will broadly fund site visits at champion developments around Europe and organize conferences on research in biobanking technology. **(**All)

Deliverables

D2.2.1: Exploring existing and desired technological solutions. (m18)

D.2.2.2: Explore the diversity and specific requirements related to older biobank collections. Scientific report (m24)

D2.2.3: Sample handling and access procedures. Descriptive report (m36)

D2.2.4: Strategic development studies on biobanking technology: Scientific report (m42)

D2.2.5: Descriptive scientific reports from data capture task, with tentative recommendations and design of pilot studies for evaluation of biomarkers of quality. Scientific reports (m36)

D2.2.6: Strategic joint research projects on biobanking per se. Scientific reports (m48)

D.2.2.7 Dissemination of knowledge detailing the results of tasks 1-8. Scientific reports (m48)

Work package 2.3

Work package number	2.3	Start date or starting event:		Mo. 1
Work package title	*Legal, ethical and societal positions*			
Activity Type	RTD			
Participant number	5	18	25	27
Participant short name	INSERM	LSG	HELEX	P3G
Person-months per participant:	24	12	12	12

The ELSI research on biobanks has focused primarily on 1) the ethical principles that should be respected when establishing such tools and infrastructures and 2) the requirements for making them operational, taking into account as a central pillar the rights of individuals [Cambon-Thomsen, 2004] . The questions of use and access were also considered in general in the light of general ethical principles, especially related to informed consent and its features, or, on the contrary, they were studied in detail in very specific contexts (isolated populations or rare diseases for example) [Knoppers 2003]. However, he ELSI picture we currently have does not cover the complexity of issues that surround the networking of biobanks and the building of biobank infrastructure. For this enterprise, new frameworks and models of governance that could apply internally to biobanks and to networking of biobanks need to be developed [Kaye, 2006; Gibbons, 2009]. However, the diversity of types of biobanks and the way that they are operated as well as how their governance systems are organized are extremely varied [Gottweiss & Petersen, 2008].

The very existence of biobanks and the move towards networks of biobanks depends very much on public trust and on the public(s) willingness to participate. However little is currently known on the views of the European citizenry on the development of biobanking infrastructure. Nothing is known about the perception by various publics of increasingly transnational ramifications of biobank projects and about the perception of the transnationalization of biobank research. While it is relatively clear how to engage citizens in debates and exchanges about national or regional biobank projects, these questions remain to be answered for projects involving multi-actor/multi-country cooperations [Avard et al. 2009]. The question of how European publics perceive, understand, and interpret BBMRI as a European infrastructure in the life sciences gains significantly of importance. Precise and reliable knowledge of the public perception of central dimensions of this infrastructure will become a key resource to interact with the European publics, but also for developing a sustainable and robust communication strategy for the DIAL-BBMRI project. In terms of strategic impact the research proposed could establish a system of monitoring and mediating the science-BBMRI-society interaction not only during the DIAL-BBMRI project, but also afterwards as the created focus group structures and networks can be easily mobilized later on.

BBMRI-PP has concentrated on identifying and developing:

- Ethical frameworks used for biobanking in the various countries of BBMRI
- Meaning of harmonization/standardization in ethics,
- Operational legal aspects to allow BBMRI to start
- Methodology for exploring the views of the European citizens and various publics on this enterprise and pilot study
- General model of governance integrating the ethical, legal and social dimensions.
- Two main kinds of biobanks were considered in BBMRI-PP: population based and clinically based biobanks. This does not cover the full range of research biobanks that may join the infrastructure.

Objectives

1. Explore the ELSI of the various access systems and uses of biobanks foreseen in the context of ERIC and biobanking infrastructure;
2. Address specific issues relevant for biobanks involving children, cord blood banking and cell lines including stem cell lines;
3. Explore the ELSI dimensions regarding the communication of results and findings to individuals and the public;
4. Document the views of the European public (s) on biobanks and their networks
5. Conceptualise a study to address how the involvement of general public or patient representatives influence the governance systems in biobanking.
6. Design a governance system for biobanking infrastructure that take into account these various dimensions

Description of work

In DIAL-BBMRI joint research WP2.3, we will build on BBMRI-PP and other works (GenbanC, PHOEBE) especially on the various relevant projects that were identified at November 2008 Brussels meeting of 25 EU funded biobanking projects[1] , in the March 2009 international conference *'Harmonizing Biobank Research: Maximizing Value-Maximizing Use* and in other biobank conferences (Oxford, 2008, Leuwen, 2009). We need to address deeply not only the construction period but to build a comprehensive well documented vision on the ELSI aspects linked to a European organized network of biobanks operating on a long term basis. These aspects concern:

- the various uses of biobanks envisaged, their combinations, their impact, taking into account present science developments,
- other domains of biobanking relevant for research than those addressed in BBMRI-PP such as: biobanking for children, cord blood biobanking for research and biobanks of cell lines possibly leading to health products; these aspects have not been addressed so far as part of a European infrastructure. Especially there is no reason why biobanks oriented towards development of cell therapy or other innovative biotherapies should not be part of the biobank and biomolecular resource infrastructure; however issues are different and legal framework of reference peculiar. It seems important to prepare to include such biobanks in BBMRI.
- the specific aspects attached to public/private partnerships need to be more thoroughly addressed
- the results generated through the uses of biobanks and their communication to the publics: the results generated from multiple uses of biobanks in the context of transnational collaboration, given the present scientific developments in several field of biology, genomics and molecular epidemiology are heterogeneous and of different kinds. They may generate changes in their nature and their impact, even for general non-individual results; joint research on such issues is needed in order to construct sound and evidence-based policies.
- the need to explore the views of citizens in various countries, thanks to the methodology identified in BBMRI-PP. . BBMRI PP has generated the basis for questions on biobanks to be posed in a Eurobarometer survey to come. We will on the one hand perform a thorough analysis of this Eurobarometer survey (quantitative survey) that will occur in 2010, including; on the other hand a qualitative survey on specific groups of publics is needed to understand the opinions and how they form and develop. This will be an essential aspect of the WP.
- the ways of involvement of various stakeholders, especially representatives of the public or patients in the different internal governance bodies and their influence must also be conceptualised.

Task 1: Mapping the ELSI of the access policies and the uses of networked biobanks

Based on documentation generated through the updated versions of the BBMRI-PP catalogue and the prototype, we will develop a position paper that will:- critically analyse the various access models at hand and compare their characteristics; study the relations between uses, access policies and expected/documented societal and scientific impact; analyse the reference framework and rationale for prioritizing the access to samples; compare the framework that governs access to samples and access to data and their practice; and assess the influence of national legal frameworks. We will organise preliminary discussion meetings with experts in the field and a workshop to discuss the position paper. This position paper will provide a basis for developing the 'supra' governance structures that need to be put in place to facilitate access to biobanks within a co-ordinated infrastructure. This will involve thorough collaboration with P3G which is leading a survey of access criteria in 50 countries as part of its new harmonization platform. We will merge the information from the different sources and will analyze together survey results and produce an "ACCESShaper" with P3G.

Task 2: Analyse the reference framework that leads to define conditions for children involvement in biobanking with transnational access in the various countries;

A number of well established principles for involvement of children are existing in reference frameworks; however lots of differences exist [Hens et al. 2009] and this area should be well studied for the different kinds of research biobanks as it seems important to have a common policy for this. The Inserm team is involved in surveying the French 20 000 children cohort being currently set up (ELFE) and this synergizes with current ongoing research on children and population biobanks in the Canadian group (Gurwitz et al., 2009). This article elicited much debate and could be the starting point for further research with the Inserm team. Problematic aspects include reconsenting the child at maturity, the return of results, withdrawal and the samples/data of minors leaving a given jurisdiction. We will perform a study comparing approaches; we will prepare a "Points to Consider" paper for this domain, circulate it and organise a discussion of this policy paper.

[1] ftp://ftp.cordis.europa.eu/pub/fp7/docs/report-meeting-eu-funded-biobanks_en.pdf

Task 3 Analyse the state of cord blood/stem cells banking for research in EU and the ethical and legal frameworks that have been applied; as most of developments have been done in relation to therapy in this domain it may be that research frameworks for this kind of biobanking is differently grounded as compared to other materials [Navarrete et al., 2009]. This will be done through web search, questionnaire survey and interviews with key persons.
Analyse the state of cell lines and stem cell lines banking for research and examine the various organizations performing this kind of biobanking in EU. Assess the need for networking and the ELSI relevance. This will involve thorough examination of the public/private partnerships and the kinds of actors involved as compared to the population and clinical biobanking . This will provide international perspectives on cord blood banking and stem cell lines for research, under the leadership of INSERM. As part of the Canadian Stem Cell Network and as the academic secretariat of the International Stem Cell Forum [Isasi et al., 2009], the Centre for Genomics and Policy (McGill) will contribute its research to date and comparative knowhow. A table comparing stem cell/cord blood banking with population/genetic biobanking and research will be prepared. Specific aspects of cell lines biobanking with potential future therapeutic developments will be analysed for their ELSI dimensions. The report will elicit areas of convergence and divergence so as to influence policy

Task 4 Survey the policies for the communication of results and findings from research conducted within biobank infrastructure
Biobanking infrastructure will link a number of biobanks over a long period of time and will involve many participants. The potential to generate research findings that will have benefits for individuals or to identify individuals with serious, treatable conditions is greatly increased. This will require new kinds of management pathways and policies that are ethical and lawful, but also are embedded in existing clinical care structures. In parallel the use of the same biobanks may lead to many findings in terms of risks that are difficult to interpret at individual level and with no individual immediate application. The development of new models for biobanking infrastructure may require a new way of communicating with research participants and may affect the way participants perceive their involvement in biobanks. Previous work has been related to implications of results for the individuals concerned or the groups; we want to explore whether new kinds of results affect the views of participants, as well as the duty of care and chain of responsibility in a way that should be taken into consideration when presenting the study and/or the results. Especially we will explore consequences of the growing development of biomarkers that objectivise a link between phenotypic dimensions across diseases in an unforeseen way, blurring the limits between diseases. This is already the case for some complex diseases (such as cardiovascular diseases and Alzheimer or autoimmune diseases for example). This may affect the views of patients on their own disease and communicating on such findings must be carefully considered. We will organize preliminary discussion meetings and a workshop to discuss the position paper. This position paper will provide a basis for developing the policies and management pathways necessary for a co-ordinated biobank infrastructure.

Task 5 Address the views of the public
This will involve quantitative, qualitative empirical research. Based on a pilot study with focus group methodology conducted in Austria and the Netherlands during 2009, the proposed WP plans to study the European perception of BBMRI along the following key dimensions: knowledge/information of and about biobanks, consent, anonymity, privacy, data protection and confidentiality, cooperation, transnational exchange between biobanks, and BBMRI as a new infrastructure. These four topics (knowledge, consent, anonymity/privacy, cooperation) have been identified in our focus group pilot study performed in Austria and Netherlands as central topics in the public perception of biobanks. In DIAL-BBMRI, we plan the following action:
The tasks will be:

- Analyse the results of the 2010 Eurobarometer survey regarding biobanks and derive a map of attitudes; this involves close **collaboration with George Gaskell (London school of economics) and the Eurobarometer** study to develop a quantitative dimension of the research. This cooperation is ongoing and the pilot study in Austria and The Netherlands has already helped to shape the questions on biobanking for a 2010 Eurobarometer survey (Leader: LSG [HG])
- Organize and perform a survey on views of citizens in several countries using a focus group approach and a common script and methodology to ensure comparability; groups will involve different publics (general, young, patient association related; participants in biobanks…) We will conduct this focus group research along the mentioned four dimensions of the perception of biobanks in different European countries. Based on Eurobarometer 2005 data (Europeans and Biotechnology 2005: Patterns and Trends, Eurobarometer 64.2, 4, 2005), attitudes towards genetic data collection range very broadly from supportive to highly critical.

Using these data as a proxy for attitudes towards biobanks, we will select Austria, Germany, Greece Luxembourg, France and the United Kingdom as cases for focus group research. These countries range from highly critical (Germany) to highly supportive (UK). The selected countries also represent a broad range of regional (north/south) difference, different levels of science understanding and knowledge, and different religious backgrounds. They will involve collaboration outside the WP.

- Analyse the results by country explored, and across countries, using Atlas (software able to deal with different languages in text analysis). This will allow a collaboration with the language and lexical tasks in WP2.1 (bioinformatics)

Task 6 Conceptualise and plan a study of the various ways stakeholders from patients groups or the general public are involved and manage their involvement in governance structures dealing with biobanks (ethics committees, access committees etc.) in different settings.
Understanding the mechanisms of active involvement of stakeholders in governance structures as compared to the attitudes in the general public is essential to policy making in this domain. Results of Task 5 will be key to explicit the parameters to study. This task will involve mainly a conceptual approach; it will allow to make precise plans and a pilot for this work, but will not be developed at large within DIAL-BBMRI because this would exceed available resources; it will be the basis of a part of an independent related project.

Task 7 Design a model of governance to be tested in the prototype
Model of governance necessarily requires distinguishing between types of biobanks, their goals, populations and the socio-ethical and legal sensitivity of the sources and of the tissues and data involved. Moreover, overly cumbersome or ill-informed governance structures can undermine the very purpose for which the participants provided tissues and data. The presence or absence of legal and professional regulatory and ethical frameworks may also determine need. Independence and financing of governance mechanisms as well as their transparency are also crucial. Considering the range of biobanks in DIAL-BBMRI, careful attention should be paid to creating range of options and their strengths and weaknesses thus allowing an informed choice of governance**.** We will pull together the various analyses carried out within this work package in order to develop models that can be used as a prototype for the governance of biobank infrastructure. We will use the empirical research performed to identify robust and accountable governance structures which will ensure public confidence and trust. Under the leadership of J K, we will prepare a schema of options with justifications and strengths and weaknesses.

Task 8 Consultation process within the research community and stakeholder forum before finalising recommendations
A series of discussion meetings coupled with consortium or other meetings will be held before we develop the final document containing recommendations for the European Commission and relevant policy making bodies.

Deliverables

D 2.3.1: Set up working groups and precise methodology on the various aspects of WP2.3 (m4)

D 2.3.2: Position paper on biobank access policies and policy options for biobank infrastructure. (ACCESShaper) (m24)

D2.3.3: Points to consider paper on biobanking children samples and data in a networked environment of biobanks (m12)

D2.3.4: Report on cord blood biobanking for research in Europe and table comparing stem cell/cord blood banking with population/genetic biobanking and research. (m30)

D2.3.5: General Report on attitudes in EU countries from the Eurobarometer survey (m12)

D2.3.6: Country reports on attitudes of EU citizens following focus groups (m24)

D2.3.7: Cross analysis of attitudes of EU citizens following focus groups and Eurobarometer (m30)

D2.3.8: Position paper on the communication of results and findings to various publics (m36)

D2.3.9: Final position paper on governance policies for biobanking infrastructure incorporating the empirical research findings as well as analysis from the position papers on children's participation, cord blood and cell lines, access models and the communication of results and findings, (m 42)

D2.3.10: Overall report on DIAL-BBMRI ELSA research (m48)

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Table 1.3 d2: Work packages description for Transnational access

Work package 3.1

Work package number	3.1	Start date or starting event:		Mo. 1			
Work package title	***Population biobank data, sample access***						
Activity Type	SUPP						
Participant number	**3**	**6**	**7**	**19**	**3**	**7**	**11**
Participant short name	NTNU	WTSI	THL	UTARTU	NTNU	THL	BBMRI-SE
Person-months per participant:	24	6	6	6	12	12	12
Participant number	**12**	**19**					
Participant short name	HMGU	UTARTU					
Person-months per participant:	6	12					

Description of the infrastructure
Name of the infrastructure: *DIAL BBMRI Population biobanks*
Location (town, country): This biobank network consists of eight prototype population biobanks located in eight different European countries. They will not differ much in internal logistic, sample handling protocols and procedures and may be treated as a single infrastructure. The main differences are related to type of biological material, sample size and related health information. Material. Access cost are similar for all biobanks
Web site address: *BBMRI.EU/biobanks*
Legal name of organisation operating the infrastructure: The legal entity of the prototype will be the same as for each corresponding partner in the table above
Location of organisation (town, country): See partner table
Annual operating costs (excl. investment costs) of the infrastructure (€): 20,9 m€
Description of the infrastructure:

The population biobanks are amongst the oldest European research infrastructures. Based on extensive initiatives to improve common health, large population based screening studies were conducted to try to reveal the most significant mechanisms for the development of cardiovascular diseases (CVD) and cancer. Preventive strategies were eventually developed based on some of the most important discoveries from these studies and cohorts. Health related information, exposure data and biological samples has thus for several decades been collected and stored in data banks and biobanks. The need for structuring and harmonization of these biobanks was one of the main arguments for the funding of the preparatory phase of BBMRI by EU.

In this preparatory phase, the strategy has been to solve the legal, governance and financial challenges involved in the Europe-wide cataloguing and storage of the vast amount of information collected in large epidemiological sample collections and population cohorts. The effort was more specifically aimed at establishing a European infrastructure for collection, storage, annotation, validation, and dissemination of the diverse data collected in national cohorts and sample collections. Such an infrastructure was also necessary to be able to facilitate the collection and storage of the biological data collected with '-omics' technologies from various platforms and diverse cell and tissue samples. This component of the biobank infrastructure has provided a unique European strength for biomedical research globally and facilitates utilization and capitalization of biobank resources by European researchers, industry and health care system.

European countries have a unique competitive strength provided by investment of tax payers and society, and the national health care systems, which have facilitated collection of clinical samples and produced highly reliable health care records. Furthermore, Europe has undeniable strengths in epidemiological studies that have data accumulated throughout decades, often complemented with biological samples. A highly beneficial feature for various research strategies is the diversity of European populations with a well established but different history. New biobanking establishments all rely on these strengths. Through BBMRI, Phoebe and the P3G, strong efforts have been put into harmonization and integration of European biobanks as well as integration of database infrastructure to maximize the leverage of the current biobanks. Novel molecular '–omics' technologies hold great promise and, if applied to analyze well characterized study samples, are mature to deliver novel

solutions critical for future health care of our societies. Recently, a strong initiative has been taken by several partners of BBMRI to organize their national hubs as standard BBMRI national infrastructures for both population based and clinical biobanks, often named as BBMRI.xx (BBMRI.nl, BBMRI.se, BBMRI.no etc.). In addition, national funding has been achieved for an increasing number of these infrastructures, strengthening the ability to operate effectively within a European biobank network as BBMRI.

The DIAL-BBMRI prototype for biobank infrastructure:

For transnational access, a population biobank prototype will all have these key features:

- The DIAL-BBMRI prototype should reflect the distributed hub and spoke architecture of BBMRI.
- Procedures should be in place for efficient transnational exchange of samples and data that properly consider the applicable ethical and legal requirements.
- The OECD best practice guidelines and the WHO/IARC guidelines for biological resource centres should serve as the basis for the construction and operation of the prototype.
- The prototype shall be based on national prototypes which are organized as hubs.
- SOPs should be available for scientific collaborations and transnational exchange of samples and data (i.e. access rules) as well as templates for MTA and CDA that consider the requirements of academia and industry
- Establishment of a common access portal for the prototype via the DIAL-BBMRI web site
- Established procedures should be suited to become integrated into the operational concept of BBMRI
- All documents generated should be made available to the BBMRI consortium

The state-of-the-art equipment and services:
We are aiming at a large-scale, cost-efficient automatized and streamlined biobanking infrastructure. Converting to automatized and streamlined processes, in conjunction with volume purchase power of consumables, we may drive down the cost for biobanking service substantially. For most sample collections, biobanking services today comprise half the cost of the entire collecting and storing endeavor. The emerging industrialization phase offers the possibility to make this part much cheaper, allowing for more added value from resources invested in medical research. This new large scale biobanking infrastructure will drive development in all areas dependent on biobanking services such as "-omics" development, research, healthcare, and the life-science industry. For all the participating countries, a strong national biobank infrastructure is also under development, creating a national hub to be part of the European BBMRI-biobank infrastructure.

Services currently offered by the infrastructure:
The main service offered by the infrastructure will be access to unique sample collections and related health information by researchers or research teams
Biosamples and data will be made available based on clear access rules, and an independent sample and data access committee (SDAC) will prioritize the applications. Specific rules for these committees must be developed, formally also involving the biobanks from where the samples are requested to such as:

- To provide financial support for access to external users. Access costs will be defined on the basis of 'user fees'.
- Transnational access to biosamples and data will be made available at very low cost to users from academia. Funding to provide transnational access will be budgeted in this project. Industrial users may also be granted access, but at a higher access fee. Sufficient compensation must be given to the prototype biobanks at request to cover their actual costs.
- To publicize widely the access offered
- Information and guidelines for transnational access will be announced through calls for proposals via the DIAL-BBMRI website and via other established channels (EU, national funders, scientific journals etc)
- To maintain appropriate documentation to support and justify the amount of access reported the use of the resource will be documented in detail in reports and on relevant web sites

There is already an widespread interest for this infrastructure with an average no of annual user between 10-20 researchers and research group. This activity may very well be enhanced by improving the infrastructure and

sample handling capacities.

Objectives

Based on the major prerequisites of European biobanks, a main objective of WP 3.1 will be to arrange for transnational access of samples from a selected numbers of prototype population biobank. These have already been defined (see above) and identified by DIAL-BBMRI as listed in the table in 2.4.
It will be necessary to ensure that all the prototype population biobanks reflect the distributed hub and spoke architecture of BBMRI. To facilitate this effort, we will further promote the organization of similar and standardized national BBMRI infrastructures to assist common procedures for access to samples.
There should be a common BBMRI prototype standard with a limited number of hubs. The biobank consortium working on a prototype hub should well coordinate its activities with other consortia and the leader of the corresponding BBMRI work package.
We will contribute to develop, harmonize and implement best practices for collection, processing, annotation, storage, and distribution protocols to ensure the highest quality samples and comparability of research results.
Vast sums have been invested in biobank infrastructures, setting prizing of samples at a level that often prevents access from common researchers. Funding of access will both provide sustainability of the prototype biobanks selected as well as promoting access from research groups
We will make sure that applicants follow the existing ethical and legal requirements.
We will also establish of a common access portal via the BBMRI web site

Description of work

Modality of access under this proposal: The access to biosamples and data will be offered to researchers from all EU member states (and associated states) including universities, research centers and industry through specific calls for proposals. European or national research projects will be selected on the basis of eligibility criteria set up by the DIAL-BBMRI. These include excellence of science, ethical criteria, and feasibility of the projects (see WP 1.9 for more details). The evaluation will be carried out by the Sample and Data Access Committee (SDAC) with the help of external experts to ensure that the process is fair and in compliance with relevant principles stated in the commission's rules[1].The selected research projects must be independently funded and must substantially profit scientifically from the use of the biobanks of the DIAL-BBMRI Prototype. Implementation of access activities and logistics will be structured in a coordinated way, to make trans-national access available to external users, through the provision of samples (see also WP.2.2).

Support offered under this proposal**:** Normally, user groups will not directly be involved in activities at the various biobank sites. Preparation of samples and specific delivery will be handle by designated personnel. Sample and data integrity will also favour a core staff at each site. The infrastructures may however offer services in further analysis of data, both scientifically and technically. This will be specifically supported by other work packages in particular WP 2.1,

Outreach of new users: During BBMRI-PP, a lot of attention has been drawn to the European biobanks as one of the most valuable resources for health related research. This is also reflected in the many high profiled publications based on biobank related material. ESF has published a science policy briefing on biobanking activities (van Ommen, Skorpen et a.2007) and several of the national research councils have released reports encouraging the use of biobanks. Through the web site of P3G (p3g.org), BBMRI-PP and from 2010, DIAL-BBMRI, we will further open up for new user groups. Web based announcements of activity and access rules will be further enhances in collaboration with WP 2.1.

Review procedure under this proposal: Fair access to samples and related clinical data. Fair access is primarily based on merit review of the proposal by the scientific and ethical committee with the help of external experts. This review will be based on a number of principles shared with the review procedure of projects used in FP7[2]. These include :

- **Excellence.** Projects selected for funding must demonstrate a high scientific quality.
- **Transparency**. Funding decisions must be based on clearly described rules and procedures, and applicants should receive adequate feedback on the outcome of the evaluation of their proposals.

[1] Rules for submission of proposals and and the related evaluation, selection and award procedures (posted on CORDIS).
[2] Rules for submission of proposals and and the related evaluation, selection and award procedures (posted on CORDIS).

- **Fairness and impartiality.** All proposals submitted to BBMTI-I3 for access to samples are treated equally. They are evaluated impartially on their merits, irrespective of their origin or the identity of the applicants.
- **Confidentiality.** All proposals and related data, knowledge and documents communicated to the scientific committee are treated in confidence9.
- **Efficiency and speed.** Evaluation, award and grant preparation should be as rapid as possible commensurate with maintaining the quality of the evaluation
- **Ethical and legal considerations:** Any proposal which contravenes fundamental ethical principles or which fails to comply with the relevant legal procedures may be excluded at any time from the process of evaluation, selection and award..

To achieve this aim WP 1.9, in close collaboration with WP 3.1 and WP 3.2, will:

- Develop a procedure to review and prioritize requests to samples and associated data
- Study the possibilities to encourage biobanks to keep an adequate supply of specimens to keep up with customer/researcher demand.
- Develop SOP, best practices and appropriate tools to increase support for the resource and investment in the quality of the resources collected and their associated data. Free access will be offered for these documents and tools.
- Harmonize cost assessment to resources, associated data and access to services and expertise.
- Implement appropriate methodology and indicators to assess the accrual of distribution to public and private partners and the impact of BBMRI-I3 on socioeconomic issues.
- Encourage researchers accessing to samples and data through BBMRI-I3 to publish their work according to Open Access paradigm.

Population biobanks will provide sample and data of individuals from the general population. Most of them are healthy, but they also include disease phenotypes. The selected biobanks address i) adults, ii) prospective data and repeated measures iii)linkage possibilities to a variety of clinical endpoints, including complex diseases

The following numbers of participants and samples are provided by population biobanks:

Populations	Subjects included	Current Samples	Additional subjects (end 2010)	Additional samples (end 2010)
Prototype Germany (Erich Wichmann)	18000	320 000		
Prototype Netherlands (Gert-Jan van Ommen)	150 000	450 000	40000	2 million
Prototype Finland (Leena Peltonen/ Markus Perola)	75000	300 000		
Prototype Norway (Kristian Hveem)	300 000	4 500 000		
Prototype Sweden (Joakim Dillner)	110 000	500000	8000	400 000
Prototype UK (Bill Ollier)			500 000	15 000 000
Prototype Estonia (Andres Metspalu)	40000	922000		
Prototype Spain (Alberto Orfao)	7500	25000		
Total	700 000	7 100 000	550 000	17.400 000

Description of work (possibly broken down into tasks), and role of partners

Tasks (Participants)

Task 1. Structuring and harmonize the prototype biobanks for transnational access by stimulating the development of common national infrastructures(All)

Task 2. Develop common access rules for all biobank prototypes, both population based and clinical(All)

Task 3. In collaboration with WP 1.7 and WP 3.1, ensure that access procedures and sample management are in

compliance with the existing ethical and legal requirements(All)
Task 4. In collaboration with WP 3.1 and WP 1.9, develop a correct prizing system to provide both sustainability of the selected prototype biobanks as well as promoting access from research groups.(All)
Task 5. In collaboration with WP 2.1, we will seek to establish a common access portal via the BBMRI web site and the implementation of a common IT-infrastructure (NTNU, HMGU)
Task 6. In collaboration with WP 1.2, WP 2.2 and WP 3.1 we will develop, harmonize and implement best practices/best quality for collection, processing, annotation, storage, and distribution protocols to ensure the highest quality samples and comparability of research results(All)
Task 7. Develop a common web based inventory and a catalogue for presentation of meta data (NTNU, HMGU, KI)

Deliverables List

D 3.1.1: Common national BBMRI biobank infrastructure for sample handling: 48 mo
D 3.1.2: Common access rules to public biobanks, population based and clinical.: 24 mo
D 3.1.3: Ethical and legal requirements for access: 24 mo
D 3.1.4: Pricing of samples and costs of access: 36 mo
D 3.1.5: Common web based solutions for access and a dynamic inventory of storage: 48 mo
D 3.1.6: QA/QC on best practices: 48 mo
D 3.1.7: Inventory, structuring of metadata: 38 mo

List of milestones

M 3.1.1: Agreement reached on common biobank infrastructure logistics for sample access: 12 mo
M 3.1.2: Consensus on access rules: 12 mo
M 3.1.3: Developed a common set of ethical an legal guidelines: 12 mo
M 3.1.4: Developing a minimal set of a common prizing system: 12 mo
M 3.1.5: Completion of first prototype of an a web based access portal: 18 mo
M 3,1,6: Collect information of existing quality standards: 24 mo

References

(1) Hung RJ, McKay et al. A susceptibility locus for lung cancer maps to nicotinic acetylcholine receptor subunit genes on 15q25. Nature. 2008 Apr 3;452(7187):633-7.
(2) Salanti G et al. Underlying genetic models of inheritance in established type 2 diabetes
(3) associations. Am J Epidemiol. 2009 Sep 1;170(5):537-45. Epub 2009 Jul 14
(4) Zeggini E et al.. Meta-analysis of genome-wide association data and large-scale replication identifies additional susceptibility loci for type 2 diabetes. Nat Genet. 2008 May;40(5):638-45.

Work package 3.2

Work package number	3.2	**Start date or starting event:**		Mo. 1			
Work package title	***Disease-biobank data, sample access***						
Activity Type	SUPP						
Participant number	**12**	**11**	**16**	**21**	**26**	**1**	**2**
Participant short name	HMGU	KI	EUR	TUM	UniKlu	BBMRI-NL	MedUG
Person-months per participant[1]:	30	6	6	6	6	12	12
Participant number	**5**	**12**	**20**	**28**	**9**		
Participant short name	INSERM	HMGU	USAL	ISS	UniMAN		
Person-months per participant2:	6	6	12	12	12		

Description of the infrastructure
Name of the infrastructure: *DIAL BBMRI Clinical biobanks*
Location (town, country): This biobank network consists of seven prototype clinical biobanks located in seven different European countries which may be treated as a single infrastructure. The main differences are related to type of biological material, sample size and related health information.
Web site address: *BBMRI.EU/biobanks*
Legal name of organisation operating the infrastructure: The legal entity of the prototype will be the same as for each corresponding partner in the table above
Location of organisation (town, country): See partner table
Annual operating costs (excl. investment costs) of the infrastructure (€): 27 m€
Description of the infrastructure: Clinical biobanking embraces a wide range of collection activities supporting diverse research purposes. Almost every major hospital in Europe supports collection of blood, DNA or tissues. Multicentre collections arise from clinical trials and genetic studies. Many are already organized within regional or national networks. BBMRI addresses the ongoing and future activities of clinical biobanks building on previous and current work and on international guidelines. It produces recommendations for the construction and operation of infrastructure and deals with questions of availability, quality criteria, rules of access, and incentives for participation. In the first step, existing resources, technologies, standards and know-how has been integrated into the operational concept of BBMRI. An inventory of existing biobanks and clinical sample collections in Europe that meet necessary quality standards has been made. A web-based catalogue describes each resource and its terms of access. Technical solutions and quality criteria for storage, retrieval and transfer of biological samples has been reviewed and an electronic manual of existing documents for biobanking methods is made available. This manual includes general considerations for laboratory infrastructure as well as Standard Operating Procedures covering all aspects of sample management. Currently (Status November 2009) 177 disease-oriented biobanks from 21 European countries are registered in the BBMRI Catalogue (http://www.bbmri.eu/index.php/catalog-of-european-biobanks). They offer ca 13 million samples including more than 400,000 DNA samples, 2.8 million samples derived from blood (serum, plasma, buffy coat, whole blood etc), 500,000 cryopreserved tissues, nearly 8 million paraffin embedded tissues and 300,000 cell lines **The DIAL-BBMRI prototype for biobank infrastructure:** For transnational access, the clinical biobank prototype will all have the same key features as described for population biobanks in WP3.1.

[1] except human effort already included in the calculation of the access costs.
[2] except human effort already included in the calculation of the access costs.

The state-of-the-art equipment and services:
We are aiming at a large-scale, cost-efficient automatized and streamlined biobanking infrastructure as described for population biobanks in WP3.1.

Services currently offered by the infrastructure:

The main service offered by the infrastructure for clinical biobanks will be access to unique sample collections and related health information by researchers or research teams, as described for population biobanks in WP3.1.

Objectives

WP 3.2 wants to foster collaboration, harmonizing and networking of clinical biobanks. These can be used to discover or validate genetic and non-genetic risk factors, without having to wait for great lengths of time and spend large efforts on longitudinal, prospective collection. When follow-up information is available, this will allow to recognize chronic disease profiles against a background of naturally occurring variations. In addition, and in particular when enriched with state-of-the-art biological samples and data, these biobanks are invaluable for discovering biomarkers, and for studying factors influencing disease progression, mortality and responses to treatment. The objective of this work package are (a) to develop a long-term, strategic vision of the role and place of clinical biobanks at the interface between clinical practice an research; (b) to provide solutions for networking biobanks in a way that maximizes the opportunities for the discovery of new biomarkers and their validation and translation towards clinical applications; (c) to provide support for the development of a European framework facilitating harmonization of standards through certification and accreditation procedures.

WP 3.2. will address the ongoing and future activities of clinical biobanks. It will provide access to a selected number of large, high-quality biobanks which have already a lot of experience with successfully offering biosamples and data to external users. Via the I3-Prototype these biobanks provide samples for common, frequent diseases to allow a maximum potential for usage. Furthermore, we received letters of interest from ongoing large European research projects which would profit substantially from the use of the biobanks in the I3-Prototype we can offer. However, the I3-Prototype is also available for other researchers. The main criteria for access is quality of the research proposal, ethical related issues and feasibility of the project. This will be evaluated by an the scientific and ethical advisory committee with the help of external experts, see WP 1.9.

WP 3.2 will closely cooperate with BBMRI WP 2.1 which is focussing on interoperability and multilingual knowledge retrieval. WP 2.1 will provide concepts, IT solutions and tools for integration and knowledge management. WPs 5 and 3 of BBMRI PP have already successfully developed a portal system and an integration prototype. By extending the PP concepts and solutions, WP2.1 will realize a service-oriented architecture and a federated database in close cooperation with national projects. This architecture will include a terminology mapping service based on an online multilingual Biobank terminology system.

Description of work

Modality of access under this proposal: The access to biosamples and data will be offered to researchers from all EU member states (and associated states) including universities, research centers and industry through specific calls for proposals, as described for population biobanks in WP3.1.

Support offered under this proposal**:** see WP3.1

Outreach of new users: see WP3.1

Review procedure under this proposal: see WP3.1

Clinical biobanks will provide samples and data from patients. The selected biobanks address four groups of frequent diseases

1) Cancer (lip, tongue, salivary glands, floor of mouth, oral cavity, mesopharynx, nasopharynx, hypopharynx, pharynx, oesophagus, stomach, intestines, colon, rectum, liver, pancreas, peritoneum, nose-sinuses**, .**larynx, lung, pleura, mediastinum, breast, cervix, corpus uteri, ovaries, prostate, testis, kidney, bladder, melanoma, skin, eye, brain, thyroid, endocrine, bone, connective tissue, etc)

2) Neurodegenerative diseases (Parkinson's, Alzheimer's, dementia, multiple sclerosis, migraine, cluster headache, etc)

3) Cardiovascular disease and diabetes (myocardial infarction, heart failure, hypertension, coronary heart disease, type 1 and type 2 diabetes)

4) Immunological and infectious diseases (HIV/AIDS, Sepsis, asthma, allergy, celiac disease, inflammatory bowel disease, rheumatoid disease, psoriasis, infection/resistance)

These fields are chosen because a large number of European research projects are ongoing and can profit from the I3-Prototype.
The following numbers of participants and samples are provided by clinical biobanks

Clinical biobanks patients	Cancer	Neuro	Cardio/ Diabetes	Immunology/ Infections	Total No. patients
Prototype Germany (Erich Wichmann)	2000	6000	15000	15000	38000
Prototype Netherlands (Gert-Jan van Ommen)	30000	10000	80000	37000	157000
Prototype Austria (Kurt Zatloukal)	1 000 000	-	-	-	1 000 000
Prototype UK (Bill Ollier)	10000	4000	7500	-	22000
Prototype Spain (Alberto Orfao)	35000	1500	5500	4000	46000
Prototype Italy (Giovanni Migliaccio)	35000	5000	2500	5000	48000
Prototype France (Georges Dagher)	35000	80000	35000	3000	153000
Total	1.200 000	110 000	150 000	70000	1 500 000

Clinical biobanks samples	Cancer	Neuro	Cardio/ Diabetes	Immunology/ Infections	Total No. Samples
Prototype Germany (Erich Wichmann)	10000	33000	72000	75000	190000
Prototype Netherlands (Gert-Jan van Ommen)	90000	30000	240000	110000	470000
Prototype Austria (Kurt Zatloukal)	3 700 000	-	-	-	3 700 000
Prototype UK (Bill Ollier)	10000	8000	19000	-	37000
Prototype Spain (Alberto Orfao)	72000	3000	16000	30000	121000
Prototype Italy (Giovanni Migliaccio)	400000	16000	4000		420000
Prototype France (Georges Dagher)	930000	170000	230000	30000	1 360 000
Total	5 100 000	260000	580000	250000	6 200 000

Tasks (Participants)
Task 1. Structuring and harmonize the prototype biobanks for transnational access by stimulating the development of common national infrastructures(All)
Task 2. Develop common access rules for all biobank prototypes, both population based and clinical(All)
Task 3. In collaboration with WP 1.7 and WP 3.1, ensure that access procedures and sample management are in compliance with the existing ethical and legal requirements(All)
Task 4. In collaboration with WP 3.1 and WP 1.9, develop a correct prizing system to provide both sustainability of the selected prototype biobanks as well as promoting access from research groups.(All)
Task 5. In collaboration with WP 2.1, we will seek to establish a common access portal via the BBMRI web site and the implementation of a common IT-infrastructure (NTNU, HMGU)
Task 6. In collaboration with WP 1.2, WP 2.2 and WP 3.1 we will develop, harmonize and implement best practices/best quality for collection, processing, annotation, storage, and distribution protocols to ensure the highest quality samples and comparability of research results(All)

Task 7. Develop a common web based inventory and a catalogue for presentation of meta data (NTNU, HMGU, KI)

Deliverables List

D 3.2.1: Common national BBMRI biobank infrastructure for sample handling: 48 mo
D 3.2.2: Common access rules to public biobanks, population based and clinical.: 24 mo
D 3.2.3: Ethical and legal requirements for access: 24 mo
D 3.2.4: Pricing of samples and costs of access: 36 mo
D 3.2.5: Common web based solutions for access and a dynamic inventory of storage: 48 mo
D 3.2.6: QA/QC on best practices: 48 mo
D 3.2.7: Inventory, structuring of metadata: 38

List of milestones

M 3.2.1: Agreement reached on common biobank infrastructure logistics for sample access12 mo
M 3.2.2: Consensus on access rules: 12 mo
M 3.2.3: Developed a common set of ethical an legal guidelines: 12 mo
M 3.2.4: Developing a minimal set of a common pricing system: 12 mo
M 3.2.5: Completion of first prototype of an a web based access portal18 mo
M 3.2.6: Collect information of existing quality standards: 24 mo
M 3.2.7: Agreement on structure of common inventory/Meta data catalogue: 36

Implementation plan

Short name of installation	Unit of access	Unit cost	Min. quantity of access to be provided	Estimated no of users pr year	Estimated number of days spent at the infrastructure	Estimated number of projects/ year
All prototypes	Handling and shipment of any sample	€ 2500		10	Not relevant	10
All prototypes	Urine	€5 (2-7) /1 ml	smaller volumes or amounts may also be relevant where the requested resource is limited or the actual analysis requires less	10	Not relevant	10
All prototypes	Serum	€5 (2-7) / 0.1 ml		10	Not relevant	10
All prototypes	Plasma	€5 (2-7)/ 0.1 ml		10	Not relevant	10
All prototypes	DNA	€5 (2-7)/ µg		10	Not relevant	10
Limited	RNA	€5 (2-7)/sample		10	Not relevant	10
Selected no of biobanks	Immortalized cells	€ 50	To be negotiated	1-2	Not relevant	1-2
Selected no of biobanks	Immortalized Cell lines	€ 200	To be negotiated	1-2	Not relevant	1-2
Clinical biobanks	Tissue paraffin embedded or cryopreserved	€ 500 (200-700) per sample	excluded infrastructure, operation and attrition	4-5	Not relevant	4-5

Access costs:

Type	Price (€)	Comments
Blood and Urine	€ 2500	handling and shipping
Urine	€5 (2-7) per 1 ml	smaller volumes/amounts may also be relevant where the requested resource is limited or the actual analysis requires less
Serum	€5 (2-7) per 0.1 ml	as above
Plasma	€5 (2-7) per 0.1 ml	as above
DNA	€5 (2-7) per µg	as above
RNA	€5 (2-7) per sample	as above
Immortalized cells	€ 50	Volume to be negotiated
Immortalized Cell lines	€ 200	
Tissue paraffin embedded or cryopreserved	€ 500 (200-700) per sample	Exc. infrastructure, operation and attrition

Costs (see section 2.4 of this document).

Contingency plan

The immediate strength of DIAL-BBMRI will be that it both builds on an existing and successful EU-infrastructure, BBMRI-PP, as well as offering access to well established, fully equipped and comprehensive prototype biobanks. For transnational access activity, contingency is therefore less likely to occur. The wide spread and disseminated infrastructure will have sufficient redundancy to counteract a situation where some of the participating biobanks may face a termination of activity. Funding allocated to these biobanks may effectively be distributed to others with the ability to increase their delivery.
Ideally, the joint research activity planned to enhance automation and high-throughput sample handling activity, will substantially improve the infrastructure, but in case of prolonged manual handling, we will still be able to fulfil our access obligations.

Table 1.3 e: Summary of staff effort

Part no./short name	WP 1.1	WP 1.2	WP 1.3	WP 1.4	WP 1.5	WP 1.6	WP 1.7	WP 1.8	WP 1.9	WP 2.1	WP 2.2	WP 2.3	WP 3.1	WP 3.2	Total person months
1. LUMC	72		4							72				(+12)	160
2. MedUG	4				24					24				(+12)	64
3.NTNU	4					4		4	4		24		24(+12)		76
4. UTU	36				12										48
5. INSERM	4			12			5	4	12			24		(+12)	73
6. WTSI	12					4							10		26
7. THL	4					4				24			6 (+12)		50
8. IPRI	4			24	4										32
9. UniMan	4	4		12				12			6			(+12)	50
10. ULEIC	4	12			4	4				12					36
11. KI	4							4		96	6			6(+12)	128
12. HMGU	4	4				4			4				(+12)	30(+6)	58
13. BBT	4		24						4						32
14. Legal P.							12								12
15. NIPH	4	4		12		12									32
16. EUR				12										6	18
17. deCODE										12					12
18. LSG				12								12			24
19. UTARTU	4			12									6 (+12)		34
20. USAL														(+12)	12
21. TUM										48				6	54
22. UU			8												8
23. SLU			8												8
24. IPPOSI	18			6	12										36
25. HeLEX						4						12			16
26. UniKlu										48				6	54

27. P3G		12				8						12			32
28. ISS														(+12)	12
Total	186	36	44	102	56	44	17	24	24	336	36	60	100	132	1197

Between brackets are the person months that are reserved for and to be distributed to the biobanks that give access (in case of a distributes infrastructure).

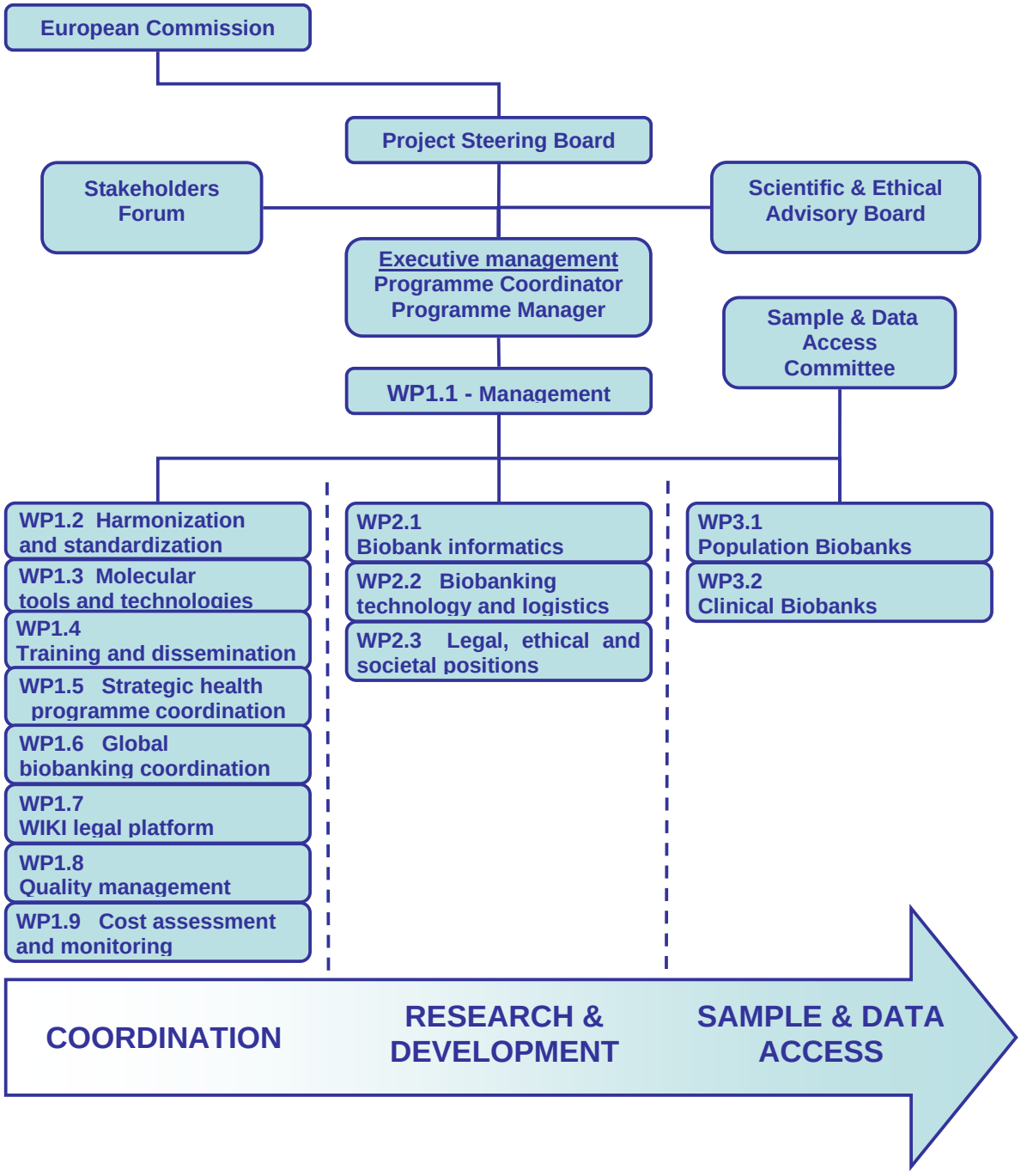
2. Implementation

2.1 Management structure and procedures

To allow DIAL-BBMRI to achieve its objectives, particular care has been taken to devise a coherent management structure. Specifically, it has been framed according to these interlinked objectives:

- To implement decision-making, quality control and conflict resolution mechanisms
- To provide timely and efficient contractual, scientific, financial and administrative coordination of DIAL-BBMRI
- To conduct a comprehensive evaluation of the Consortium's performance at regular intervals
- To ensure timely and high-quality execution of DIAL-BBMRI

Figure 3: Management structure



Project Coordinator (PC)

The project is led and managed by Prof Dr Gert-Jan van Ommen**,** from Leiden University Medical Center where he is head of the Department of Human Genetics. He is a well-known molecular geneticist, having as main research interests neuromuscular and neurodegenerative diseases (with a focus on Duchenne Muscular Dystrophy and Huntington Disease); the development and application of genomics, diagnostic technology and therapeutic strategies for genetic diseases. He has published over 340 papers in peer-reviewed journals, with 18.000 citations, with 24 of the 35 papers receiving over 100 citations originating from his own group. Prof. van Ommen has extensive experience with the coordination of large national and international consortia, and is well-placed to take the lead of DIAL-BBMRI. In his position, he has obtained funding for, participated in and/or coordinated large national and international studies and consortia, including, nationally, CMSB (www.cmsb.nl), CBG (www.biomedical-genetics.nl) and BBMRI-NL (website under construction), and internationally GenomEUtwin, Gen2Phen, EuroGENtest, BioSapiens, P3G, ENGAGE, Concept Web Alliance, BBMRI and ELIXIR. Recently the joint work of his group and the Leiden Biotech company Prosensa has led to successful proof-of-principle of antisense-based therapy for DMD, which has led to a joint development contract between Prosensa and GSK with a total value of 680 M$. Prof van Ommen also has a broad track record in the presentation, to the public and professionals, of societal aspects of genetic advances.

In these projects, he has been involved in all stages of many studies, including the early phases of establishing the protocol, through the intermediate phase of monitoring study progress, and the later phases of analyzing the data and preparing manuscripts. His involvement in these studies involved him in numerous collaborations with researchers worldwide. His position as Project Coordinator has the approval of all project Participants.

The PC is responsible for the control and implementation of the project, including legal and administrative aspects. The PC will chair regular management meetings and coordinate technical activities across the project. The control of finances is managed by the PC is based on the Consortium Agreement (CA). The CA specifies in detail the rules for the distribution of pre-payments to the Consortium Participants.

Tasks and responsibilities

- Day-to-day legal, contractual, ethical, financial, administrative and technical management of the Consortium
- Preparing, updating and managing the CA between the participants
- Scientific coordination: monitoring and assessing progress, overseeing tasks and milestones
- Monitoring and assessing risks identified by the Project Board and ensuring contingency plan implementation
- Assuring integration of WPs and direct liaison with the WP Leaders
- Supervision of and submission to EC of annual reports
- Obtaining audit certificates from each of the participants
- Managing the overall budget
- Regular reporting to and liaison with the EC Project Officer
- Responsible for the internal and external relations of the Consortium

Management Support is set up through an Executive Management, involving the PC and the Project Manager:

The Project Manager (PM) provides close monitoring of actions and Deliverables, ensures detailed information sharing between the Participants, collects and assembles data to effectively monitor progress and costs, assists the WP Leaders in setting and monitoring detailed milestones and objectives, and provides logistical support to the PC. The prospective PM has extensive experience in the management of international, multi-disciplinary, large-scale projects, including EC projects

Tasks and responsibilities

- Day-to-day coordination and administration
- Follow-up of work schedules and issuing reminders for task initiation or completion
- Development the project's identity and disseminate the identity components and guidelines for their use to the Participants

- Chairing the Project Steering Board meetings
- Distribution of Reports and drafting and distribution of meeting minutes
- Setup and running public and internal website
- Organization of meetings and workshops
- Implementation of dissemination and networking
- Communication with the European Commission
- Close follow up of legal, contractual and financial issues

The PM participates in meetings and phone conferences, and will also be in frequent contact with all Participants and the European Commission through email to ensure consistent involvement of the project's participants.

Project Steering Board (PSB)

The PSB is the Consortium's highest decision-making body. It is setup by all WP leaders.
The PSB will have the following members:

- PC
- Each WP Leader
- PM, chair of the Board

The PSB is responsible for monitoring the overall progress direction of the project, the resources used and the costs incurred, and decides on implementation issues. Any deviations from stated project plans will be assessed and decided upon by the PSB, and passed to the PC to liaise with the European Commission Project Officer. The PSB will act as a mediatory body to address any differences between participants in case they arise.

Tasks and responsibilities

- Coordinate the technical activities of the project, strategic orientation of DIAL-BBMRI Biobank and address any issue concerning the proper operation of the Consortium
- Coordination of progress, cooperation and inter-working between the WPs and different activities
- Development and implementation of a Risk Management Strategy (RMS) to address potential risks and contingency plans those identified
- Formulate and monitor the Plan for Use and Dissemination of foreground (knowledge)
- Oversee Science and Society issues related to the activities conducted within the project
- Management of knowledge (foreground and background) by ensuring all Intellectual Property Rights (IPR) are respected
- Reviewing all project Deliverables (including annual reports) prior to making them available outside the project Consortium, ensuring a two-stage review procedure, i.e. reviewed firstly within the WP and secondly the PSB
- Confer upon the structure and content of the annual scientific and management reports
- Monitor and decide on the evolution of the Consortium

All high level technical decisions will be taken within the PSB. In terms of reaching agreements, each PSB member, with the exception of the PM, has a voting right. Any key decision to be made will require clear presentation of reasons and impact on the project timing and objectives. In the unlikely case where a consensus is still not possible, the PC will have a casting vote. The decision making process will be specified in the Consortium Agreement. Participation in the PSB is mandatory for all the Representatives. When a Representative cannot attend a PB meeting, he/she may give power to another Representative from the same organization, to represent him/her.

In addition to bimonthly telephone conferences, the PSB will meet at least physically at the occasion of the Annual General Meeting (AGM) where WP leaders will present progress of their work in the form of a presentation and printed report, to allow assessment of progress against plan, risk assessment, and evaluation of technical direction. External subject matter experts will be invited to participate in these meetings where necessary. The PSB meetings and discussions will follow a written agenda distributed in advance of the each meeting. Minutes will be taken by the PM and published in a timely manner in the private area of the project website.

Annual General Meeting (AGM)

For optimal coordination, dissemination of scientific and logistic advances and improvement of networking, a yearly meeting of all the PI's will be held, to be attended by a number of relevant senior scientists from the participating institutions.

Work package leaders (WPL)

Work to be done is divided into WPs, each of which is under the direct control of a WPL. The WPL is responsible for the appropriate implementation of their assigned WP tasks and the continuous monitoring and recording of effort, progress, and expenditure in relation to their WP.

Tasks and responsibilities

- Coordinate the scientific work and implementation of the defined WP tasks
- Monitor and managing the performance of each Participant within the WP
- Delegate tasks to WP members when necessary
- Initiate and ensure open communication between WP members for WP related tasks
- Liaison with the PM, in particular for Immediate reporting of any concerns
- Provide the PM with a Progress Report (PR) every 6 months
- Ensuring and submitting to the PM the Deliverables within specified time and budget
- Identifying any new knowledge (foreground) generated by their WP and explore how that knowledge can be exploited
- Provide input on opportunities for dissemination activities
- Monitor the relevant Deliverables and milestones and report delays and problems to the PSB.

The communication frequency and mode between the WPL with other Participants in WPs will be determined by the specific needs in each WP, and in collaboration with the PSB. Communication will be mainly by phone and email. WP will come together once every three months, either physically or telephone conference link, depending on the meeting agenda, with at least one annual physical WP meeting, and more often if needed. WP meetings can take place on the occasion of PSB meetings. With an emphasis on WP integration elements, each WPL will report on progress, raise any technical or scheduling issues, and apprise themselves of the overall progress of the work. The PM will attend the meetings and keep minutes that will be made available to all Participants on the private area of the project website.

Scientific and Ethical Advisory Board (SEAB)

A number of leading Scientists in relevant fields will make up the Scientific and Ethical Advisory Board (SEAB). The SEAB will provide advice and feedback on project decisions and direction, via attendance of the annual general meeting and in-board discussions with the WPL, PM and PC, to be reported to the PSB through its chair.
In principle the SEAB of the BBMRI-PP project will be the core of the DIAL-SEAB. This board consists of Karima Boubekeur (Hoffmann-La Roche Ltd, CH), Jean-Jacques Cassiman (EuroGENtest, BE), David R. Cox (Perlegen Sciences, USA), Mark J. Daly (Broad Institute, Harvard, MIT, USA), Klaus Lindpaintner (F. Hoffmann-La Roche AG, CH), Bela Melegh (University of Pecs, HU), Lyle J Palmer (University of Western Australia).
Prof. Gert-Jan van Ommen, who was the SEAB's chair, is the current PC and for the sake of impartiality another chair will be chosen between the SEAB members. Prof Bartha M. Knoppers (McGill University, Montreal, CA), past SEAB member, has now joined as participant and will be replaced with a high-level scientist with similar expertise. The complete SEAB group will be defined during the first 2 months of the project. The SEAB members will be reimbursed for expenses for travel and subsistence, which will facilitate their participating in project meetings. The PM will manage this travel and subsistence budget.

Stakeholder Forum (SF)

The Stakeholder Forum (Chair: Michael Griffith, IE) collates the input and requirements of the broad and heterogeneous stakeholder community of BBMRI, comprising patients, clinicians, funding organizations, associated project partners, industry, and users. Continuing from the BMRI-PP fort the sake of consistency and stability, the Stakeholder Forum conference will be the central element in the public consultation process. A

specific web-site section of BBMRI will be set up for stakeholders where relevant information will be provided and stakeholders are invited to submit comments. Furthermore, a Stakeholder Training Course will be held as a further extension of the public consultation process.

Sample and Data Access Committee (SDAC)

The Sample and Data Access Committee (SDAC) will have six members and a chair, and will be selected from five members from different work packages and two external experts. Members will have two-year terms, once renewable, and in the first year a rotation schema will be established.

2.2 Individual participants

Partner 1 – Leiden University Medical Centre (LUMC), NL – Lead contacts: Prof. dr Gert-Jan B van Ommen and Dr. Barend Mons

Leiden University Medical Centre (LUMC, http://www.lumc.nl) is a center for medical innovation, committed to the advancement of health care. Its focus is on translational research to accelerate the trajectory from the laboratory findings to clinical application and into the market place. As one of the seven academic medical centers it provides patient care and medical education. LUMC performs 12,000 daytime treatments and 20,000 hospital admissions yearly, has 800 beds and employs 7,500 people. It hosts the Leiden Genome Technology Center (LGTC), the main genomics technology facility in the Netherlands, and maintains the Leiden Open Variation Database (LOVD) an open-source system in use at 750 locations worldwide for locus-specific mutation and phenotype annotation. LUMC participates in the Pearl String Initiative, the prospective biobanking initiative initiated by the Netherlands Federation of University Medical Centers (NFU) and funded by the Netherlands Government (35 M€) and is the coordinating site for BBMRI-NL, the Dutch biobanking hub funded by the Government (22.5 M€).

Prof. Gert-Jan van Ommen is head of the Department of Human Genetics, which is the seat of LGTC and LOVD. He has a long standing experience in the genetics of rare and common diseases, including therapy development. He is Editor in Chief of the European Journal of Human Genetics and is (co-) author of over 340 papers in peer-reviewed journals, with 18.000 citations, with 24 of the 35 papers receiving over 100 citations originating from his own group. His main research interests are in neuromuscular and neurodegenerative diseases (with a focus on Duchenne Muscular Dystrophy and Huntington Disease); the development and application of genomics, and diagnostic technology to rare disease research and biobanking, and therapeutic strategies. Recently the joint work of his group and the Leiden Biotech company Prosensa has led to successful proof-of-principle of antisense-based therapy for DMD, which has led to a joint development contract between Prosensa and GSK with a total value of 680 M$. He also has extensive expertise in the coordination of international organizations and the management of large research projects. He has been president of HUGO, the European Society for Human Genetics and the Dutch Society for Human Genetics, and is director of the Center for Medical Systems Biology (CMSB), one of the two trans-institutional, health-oriented genomics centers funded by NGI. He is treasurer of P3G and was one of the founding members of the European Biobanking Infrastructure BBMRI. He participates in many current and past international projects in the field of genetics, bioinformatics and biobanking, including GenomEUtwin, Gen2Phen, EuroGENtest, BioSapiens, P3G, ENGAGE, Concept Web Alliance, BBMRI and ELIXIR.

The Biosemantics group, lead by Dr. Barend Mons (PhD 1986) has been one of the early drivers of concept-based text and data mining. The group has made significant contributions to our ability to remove ambiguity from texts by mapping terms and identifiers to internationally accepted standard identifiers, and has subsequently specialised on using reasoning with the association between concepts to discover new knowledge and on the role of the community in annotation of global public information. Currently, the group is a leading collaborator in the international Concept Web Alliance and the work done in the context of this proposal will benefit broadly from the collaborations in this Alliance, such as with the National Center for Biomedical Ontology in the United States, but also the Latin American and Caribbean Center for Health Information (BIREME) in Brazil and ORPHANET in Paris, which are partners specialising in cross-language provision of health information. For BBMRI, the Biosemantics group will focus in the semantic interoperability of Biobanking information throughout Europe. Dr. Mons has spent more than a decade in fundamental cellular and molecular biology aspects of malaria, before moving to the European Commissions Research Directorate for three years as a Seconded National Expert. After his return to The Netherlands, he initiated the BioSemantics group, first at the Erasmus University and later also at the Leiden University Medical Center. During his last decade of research he published extensively on concept-based text mining and its role in biological research and the semantic web. He

also founded two spin-off companies in this field. Barend Mons brings extensive international networking expertise in cross lingual information matching to the team.
The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Gert-Jan van Ommen, PhD	Professor, LUMC	Genomics, DNA diagnostics, therapy development, rare diseases, societal impact
Johan den Dunnen, PhD	Professor, LUMC	Genomics technology, mutation analysis, database development, next-gen. sequencing
Judith Boer, PhD	Senior Scientist LUMC	Oncogenetics, bioinformatics, biostatistics, high-density data integration
Peter-Bram 't Hoen, PhD	Senior Scientist LUMC	Functional genomics, seq. based transcriptomics, high-density data integration, text mining
Barend Mons, PhD	Associate professor, LUMC	Text mining, semantic web, annotation
Marco Roos, PhD	Senior researcher, LUMC	Workflows, e-science
Dmitry Katsubo, MSc	Software engineer (NBIC)	Software engineering, project management
TBD (other project)	Software engineer, LUMC	Text mining, semantic web

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
	van Ommen
1	Van Deutekom JC, et al. 2007. Local dystrophin restoration with antisense oligonucleotide PRO051. N Engl J Med.;357(26):2677-86.
2	van Ommen GJB and Cornel MC. Recreational genomics? Dreams and fears on genetic susceptibility screening. European Journal of Human Genetics (2008) 16, 403–404
3	t Hoen, P. A., et al.. 2008. Deep sequencing-based expression analysis shows major advances in robustness, resolution and inter-lab portability over five microarray platforms. Nucleic Acids Res 36:e141.
4	Bruder, C. E., et al. 2008. Phenotypically concordant and discordant monozygotic twins display different DNA copy-number-variation profiles. Am J Hum Genet 82:763-71.
5	Aartsma-Rus, A., et al.. 2009. Guidelines for antisense oligonucleotide design and insight into splice-modulating mechanisms. Mol Ther 17:548-53.
	Mons
1	Altman RB, Bergman CM, Mons B et al. Text mining for biology - the way forward: opinions from leading scientists. Genome Biology, 2008, Sep 1, 9(Suppl 2):S7
2	Jelier R, 't Hoen PAC, Sterrenburg E, Mons B et al. Literature-aided meta-analysis of microarray data: a compendium study on muscle development and disease. BMC Bioinformatics, 2008, Jun 24, 9(1):291
3	Mons B, Ashburner M, Chichester C, et al. Calling on a million minds for community annotation in WikiProteins. Genome Biology, 2008, May 28, 9(5):R89
4	Schuemie MJ, Mons B, Weeber M et al., Evaluation of techniques for increasing recall in a dictionary approach to gene and protein name identification, Journal of Biomedical Informatics, 2007, Jun, 40(3):316-24
5	van Bemmel JH, van Mulligen EM, Mons B, et al., Databases for knowledge discovery. Examples from biomedicine and health care., International Journal of Medical Informatics, 2006, Mar-Apr, 75(3-4):257-67

Partner 2 – Medical University of Graz (MUG), Austria – Lead contact: Dr. K. Zatloukal.

The Medical University of Graz (MUG) is associated with the University Clinics of Graz, with 1600 beds and 78000 patients/ year. This facilitates close integration of research and routine clinical services. An important asset of the MUG established in an integrated setting of clinical routine and latest medical research is its ISO-certified biobank core-facility, hosting 3.1 million formalin-fixed paraffin-embedded (FFPE) and more than 120,000 cryopreserved tissue samples and 350,000 serum samples from in total 1.2 mio patients, which according to the BBMRI questionnaire is the largest collection in Europe. The resources are complemented by latest morphological technologies (Laser capture microdissection, LSM, electron microscopy), SPF facility for animal experiments (tumor xenografts and transgenic models) and ISO-certified RNA and DNA analysis (real-time PCR, DNA microarrays, 454-sequencing) as well as proteomics and metabolomics (lipidomics) platforms. All these research resources of the Medical University of Graz are centralized in the Organisational Unit for

Research Infrastructure and operated by first class permanent core facility staff comprising of experienced scientists and skilled technicians.
Kurt Zatloukal is professor of Pathology and coordinates the preparatory phase of a European biobanking and biomolecular research infrastructure (BBMRI) within the 7th EU framework programme. BBMRI should provide access to high quality human biological samples to enable future needs of large genetic epidemiology and sequencing studies. In this context it is crucial to establish Europe-wide harmonized processes and quality criteria that are compliant with the requirements of latest -omics technologies as well as with ethical and legal regulations. He also leads in the FP7-funded large integrated project SPIDIA the development of new European standards and norms for pre-analytical processing of tissue samples. In the context of the Austrian Genome Programme and several nationally funded projects the group of K. Zatloukal has developed innovative solutions for extraction of data from medical records, data integration, data clean-up and visual analytics.
Kurt Zatloukal was member of the OECD task force on biological resource centres and the Roadmap Working Group of the European Strategy Forum on Research Infrastructures. Moreover, he is member of the steering committee of the P^{3}G consortium, contributed to the OECD best practice guidelines for biological resource centres, the regulations for genetic testing of the Austrian Gene Technology Law, and the opinion on Biobanks for research of the Bioethics Commission at the Austrian Federal Chancellery.
Andreas Tiran is associated Professor of Laboratory Medicine and Director of the Organisational Unit for Research Infrastructure. He coordinates central research resources and core facilities services and takes main responsibility for quality management certification according to ISO 9001:2008. Andreas Tiran also is coordinator of the Austrian Biobank Network.
The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Kurt Zatloukal	Professor of Pathology, MedUG	Biobanking, Molecular pathology
Andreas Tiran	Director of Organisational Unit for Research Infrastructure, MedUG	Biobanking, Laboratory Medicine
Heimo Mueller	PhD, MedUG	Visual data analytics, biocomputing
Christian Viertler	MD, Researcher, MedUG	Biobanking, sample collection and pre-analytics

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Haybaeck J, et al. A lymphotoxin-driven pathway to hepatocellular carcinoma. Cancer Cell. 2009 Oct 6;16(4):295-308. PubMed PMID: 19800575.
2	Streit M, et al. Bioinformatics. 2009 Oct 15;25(20):2760-1. Epub 2009 Jul 20. PubMed PMID: 19620095; PubMed Central PMCID: PMC2759551.
3	Schweiger MR, et al. Genome-wide massively parallel sequencing of formaldehyde fixed-paraffin embedded (FFPE) tumor tissues for copy-number- and mutation-analysis. PLoS One. 009;4(5):e5548. Epub 2009 May 14. PubMed PMID: 19440246; PubMed Central PMCID: PMC2678265.
4	Gebeshuber CA, Zatloukal K, Martinez J. miR-29a suppresses tristetraprolin, which is a regulator of epithelial polarity and metastasis. EMBO Rep. 2009 Apr;10(4):400-5. Epub 2009 Feb 27. PubMed PMID: 19247375; PubMed Central PMCID: PMC2672883.
5	Yuille M, van Ommen GJ, et al. Biobanking for Europe. Brief Bioinform. 2008 Jan;9(1):14-24. Epub 2007 Oct 23. Review. PubMed PMID: 17959611.

Partner 3 – Norwegian University of Science and Technology (NTNU) - Norway – Lead contact: Dr. K. Hveem

The HUNT study (HelseUndersøkelsen i Nord-Trøndelag) is a comprehensive epidemiological research centre and biobank organized under the Faculty of Medicine, NTNU, Norway. It was initiated in 1984, inviting the total adult population > 20 years of age to a general, population based health screening in the county of Nord-Trøndelag, Norway (HUNT1/75 000 participants). The main emphasis was initially on hypertension and diabetes, but the scientific focus has since been substantially broadened to include a large number of health related problems and disease categories. Lately, several large, gene/environmental interactions-studies on cancer and diabetes has been conducted
In the HUNT 2 study (1995-97/75 00 participants), both serum and DNA was collected and stored. Close to 6000 of the participants have later developed an incident cancer where both clinical information and biomaterial

is available for research. In the most recent survey, HUNT 3, (2006-08/60 000 participants) the protocol for collection of biological material was significantly expanded (serum, plasma, buffy coat, cells, RNA-tubes, environmental tubes and fresh frozen urine). A strict quality standard was applied, similar to the sample handling protocol for UK biobank. In total, more than 200 000 persons have been screened through the HUNT studies. In 2006, the new HUNT biobank was established in Levanger, Nord-Trøndelag. This is a large state-of-the-art biobank, with fully automated procedures for sample handling and processing, DNA-isolation and QC, automated storage and retrieval of DNA-samples (-20 ^{O}C) as well as SNP-genotyping.
HUNT biobank also serves as a National Norwegian DNA-biobank for all major population based health surveys in Norway (the CONOR cohort), comprising almost 250 000 individuals. All samples are bar-coded and all processes are traceable through a dedicated LIMS, especially adapted for the biobank.
Our research group will be part of WP 1, lead WP 2.2 and WP 3.1, offering access to our prototype biobank. HUNT has also been actively involved as partner in BBMRI PP and in the DataSHaPER development lead by P3G and Phoebe. The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Kristian Hveem	Professor in Medicine, HUNT/NTNU	Epidemiology, Biobanking, Internal medicine
Frank Skorpen	Professor in Molecular Biology, HUNT/NTNU	Molecular biology, Genetics, Biobanking
Carl Platou	MD, Researcher, HUNT/NTNU	Genetic epidemiology, Biobanking,
Marit Næss	Chief Engineer, HUNT biobank/NTNU	Laboratory management, bio-analysis
Thor Gunnar Steinsli	IT engineer, HUNT biobank/NTNU	LIMS manager, Computing

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Hung RJ, McKay et al. A susceptibility locus for lung cancer maps to nicotinic acetylcholine receptor subunit genes on 15q25. Nature. 2008 Apr 3;452(7187):633-7.
2	Salanti G et al. Underlying genetic models of inheritance in established type 2 diabetes associations. Am J Epidemiol. 2009 Sep 1;170(5):537-45. Epub 2009 Jul 14
3	Lips EH et al , Association between a 15q25 gene variant, smoking quantity and tobacco-related cancers among 17 000 individuals. Int J Epidemiol. 2009 Sep 23.
4	Zeggini E et al.. Meta-analysis of genome-wide association data and large-scale replication identifies additional susceptibility loci for type 2 diabetes. Nat Genet. 2008 May;40(5):638-45.

Partner 4 – UTU (University of Turku, Finland) – Lead contact: Dr. Eero Vuorio

Together with the University of Graz, the University of Turku has been in charge of executive management of BBMRI-PP. In the current proposal, the executive manager of the BBMRI (E. Vuorio) will continue to supervise the progress of individual work packages, manage the flow of information between all participants (and national biobanks) together with the coordinator of DIA-EU-BBMRI, and will be responsible for reporting to the European Commission. For all meetings an agenda will be distributed, minutes will be prepared and made available to all participants. Project progress will be monitored on the basis of the pre-defined deliverables and milestones. Key players involved at the University of Turku (UTU) are Professor Eero Vuorio (currently chancellor of UTU), who will continue as a part-time executive manager of DIA-EU-BBMRI. Previously a visiting scientist and professor at the University of Chicago, at ETH-Zürich, and at the University of Texas in Houston, and of the Research Council for Health (Academy of Finland), the Chair of the European Molecular Biology Laboratory (EMBL) Council. Expert duties at the European Commission and European Science Foundation (ESF), >200 publications on molecular biology; and Dr. Heli Salminen-Mankonen, who will continue as full-time academic assistant in DIA-EU-BBMRI. Post-doctoral fellow at Imperial College and Turku Centre for Biotechnology. Coordination experience from several domestic and international projects, >25 publications.

Name	*Affiliation*	*Expertise*
Eero Vuorio, MD PhD	Professor, UTU	Molecular biology, international research management
Heli Salminen-Mankonen,	PhD, UTU	Molecular biology, biotech, project coordination

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Toronto International Data Release Workshop Authors, Birney E, Hudson TJ, Green ED, et al.

	Prepublication data sharing. Nature. 2009; 461(7261):168-70.
2	Salminen-Mankonen H, Litton J-E, Bongcam-Rudloff E, et al. BBMRI. The pan-European research infrastructure for biobanking and biomolecular resources for the future of biomedical research. EMBnet.news 2009; 15(2): 3-8.
3	English JL, Kassiri Z, Koskivirta I, et al. Individual Timp deficiencies differentially impact pro-MMP-2 activation. J Biol Chem. 2006; 281(15):10337-46.
4	Salminen-Mankonen HJ, Morko J, Vuorio E. Role of cathepsin K in normal joints and in the development of arthritis. Curr Drug Targets. 2007; 8(2):315-23.
5	Morko J, Kiviranta R, Joronen K, et al. Spontaneous development of synovitis and cartilage degeneration in transgenic mice overexpressing cathepsin K. Arthritis Rheum. 2005; 52(12):3713-7.

Partner 5 – Institut National de la Santé et de la Recherche Médicale (Inserm), France – Lead contacts: Dr. Georges Dagher (Paris) and Prof. Anne Cambon-Thomsen (Toulouse)

Inserm is a public research organization entirely dedicated to human health created in 1964, it runs a budget of 600M€, with 13 000 staff members of which 2500 MDs and 366 research units or centers. Inserm developed regional, national, European and international research networks and infrastructures in several fields. Inserm coordinates the French national network of biobanks that harbors more than 300 collections of biological resources stored in 50 centres in France. Many of these collections concern complex diseases.

Georges Dagher, PhD, is a Senior scientist with a master in anthropology. He is currently deputy director of the clinical research dept of Inserm. He is a coordinator of the French biobank network. His topics of research include hypertension, arterial hypertrophy, obesity, renal physiology. He is a member of different ethics bodies at various levels: Inserm ethics committee, Institutional review board and local ethics Committee. He is leader of WP "funding and financing" in the BBMRI project (FP7). He is national representative at various OECD committees dealing with biobanking, data bases, global network. Participation in DIA-EU-BBMRI will be in Management, Access coordination, transnational access, quality management, cost assessment and monitoring aspects (WP 1.1, WP 1.8, WP 1.9, WP 3.2)

Inserm U558, joint research unit with University Paul Sabatier Toulouse 3, entitled:" Epidemiology and analyses in Public Health" is part of a large federation of research institutes in "Health and society". The groups involved are the research team "Genomics and public health" and the "societal platform" of the genopole Toulouse Midi Pyrenees, led by Anne Cambon-Thomsen, MD, Research Director CNRS (National Centre for Scientific Research). Specialized in human immunogenetics she has a large experience in bioethics; is member of the European group on ethics (EGE). This team addresses the implications of genomics for public health, especially issues pertaining to biobanks, genetic databases and multifactorial diseases. It includes persons of different disciplinary background in biomedical sciences, social sciences and humanities. The team is involved in several EU projects (Riset, TECHGENE, GEN2PHEN, BBMRI, POSEIDON, PH2GEN and CAGEKID) with leadership on ethical and societal issues and participated in PHOEBE and GMP to GBP.

The societal platform will help managing the ELSI aspects of the project. The research team will mainly participate in ELSI aspects of several DIA-EU-BBMRI WP, notably on development of legal and ethical positions. The platform will also be implicated in training and dissemination. These WP are principally WP 1.4, WP1.7, WP 2.3). The following principal scientific /technical personnel are involved:

Name	*Affiliation*	*Expertise*
Georges Dagher	Deputy director clinical research department	Biobanking, pathology
Anne Cambon-Thomsen	Research director at CNRS	MD, Genetic of multifactorial diseases, immunogenetics, bioethics, biobanks ELSI,
Emmanuelle Rial-Sebagg	Non permanent Research fellow, Inserm	Jurist; PhD in health law on governance of biobanks; bioethics; Member of REC
Pascal Ducournau	Assistant professor of sociology, Université Albi	Sociology of health, bioethics

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Bouillier H, Samain E, Rucker-Martin C, Renaud JF, Safar M, Dagher G Hypertension. 2001 Jun;37(6):1465-72.
2	Tondu AL, Robichon C, Yvan-Charvet L, Donne N, Lelievre X, Hajduch E, Ferré P, Dugail I, Dagher G J. Biol. Chem. 2005 Sep 30; 280 (39):33536-40
3	Cambon-Thomsen A, Rial-Sebbag E, Knoppers BM. Trends in ethical and legal frameworks for the use of human biobanks. Eur Respir J. 2007. 30(2): 373-382

4	Kauffmann F, Cambon-Thomsen A. Tracing biological collections: between books and clinical trials. JAMA. 2008. 299(19):2316-8
5	Ducournau P, Cambon-Thomsen A 2009, Users and uses of the biopolitics of consent: a study of DNA banks in The ethics of research biobanking, J.H Solbakk, S Holm, B Hofmann eds, Springer-Verlag, 33-48

Partner 6 – Wellcome Trust Sanger Institute (WTSI), Hinxton - UK, Lead contact: Prof. Leena Peltonen

The Wellcome Trust Sanger Institute (WTSI) is a not-for-profit research organization and one of the foremost genome centres in the world. It contributed one third of the reference human genome sequence, has sequenced the genomes of many other species, and made significant contributions many other large international projects including the HapMap project and the WTCCC. With a faculty of 35 investigators, it is currently dedicated to the functional analysis of genomes through sequencing and other genomic techniques, human genetics and human, mouse and pathogen genetics. The Sanger Institute currently has the largest second generation sequencing capacity worldwide including 40 machines spanning three commercially available platforms. It is also currently directly involved in human genetics studies totaling over 100,000 primary samples. Genomic analysis is complemented by computational interpretation and experimental analysis of gene function in a variety of model organisms. There are designated teams for library preparation, sequencing production and data processing. The data centre for computation and data distribution has recently been extended and now has at least 3000 terabytes (Tb) of storage space available and a computer farm consisting of over 5,000 CPUs. This is the largest biological computing facility in Western Europe

Main tasks: The WTSI will be involved in all three areas of the proposal, the Networking, Joint research and Transnational access activities. We will have a role in managing the consortium and allover effort as well as in coordinating the global biobanking effort. We have already some expertise in the area of Biobank informatics which will be further developed in the joint research activity in the related work package. Beside this we will involved in the effort to provide access to data for a variety of different cohorts and studies. The following principal scientific and/or technical personnel is involved:

Name	*Affiliation*	*Expertise*
Leena Peltonen	Head of Human Genetics	in many human common and rare disease medical genetics studies, plus European cohorts
Richard Durbin	Senior Group Leader	Involved in large scale human genetics sequencing projects, including from European cohorts.
Aarno Palotie	Senior Group Leader and Head of Medical Sequencing	Involved in studies of common neurological diseases.
Nicole Soranzo	Group leader, Human Genetics and Senior Lecturer, King's College School of Medicine	Involved in studies of human common cardiometabolic disease in founder and outbred populations

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Boomsma, D., Busjahn, A., and Peltonen, L. (2002). Classical twin studies and beyond. Nat Rev Genet *3*, 872-
2	Nousiainen, H.O., Kestila, M., Pakkasjarvi, N., et al. (2008). Mutations in mRNA export mediator GLE1 result in a fetal motoneuron disease. Nat Genet *40*, 155-157.
3	Yuille, M., van Ommen, G.J., Brechot, C., et al. (2008). Biobanking for Europe. Brief Bioinform *9*, 14-24.
4	Aulchenko, Y.S., Ripatti, S., Lindqvist, I., et al. (2009). Loci influencing lipid levels and coronary heart disease 16 European population cohorts. Nat Genet *41*, 47-55.
5	Sabatti, C., Service, S.K., Hartikainen, A.L., et al. (2009). Genome-wide association analysis of metabolic tra birth cohort from a founder population. Nat Genet *41*, 35-46.

Partner 7 – National Institute for Health and Welfare (THL), Finland – Lead contact: Dr. Markus Perola

The National Institute for Health and Welfare (THL) is a research and development institute under the Finnish Ministry of Social Affairs and Health. THL works to promote the well-being and health of the population, prevent diseases and social problems, and develop social and health services. Since 2006, the Public Health Genomics Unit of THL is part of Institute for Molecular Medicine Finland (FIMM), a joint EMBL-associated

research institute between the University of Helsinki, the National Institute for Health and Welfare (THL), the University Hospital (HUS) and VTT Technical Research Centre of Finland. FIMM aims to advance new fundamental understanding of the molecular, cellular and etiological basis of human diseases using unique Finnish and European population and clinical sample resources. The centralized sample collections will be stored and co-ordinated at FIMM biobanking unit.

The main areas of THL/FIMM activity will lie in WP iii and WP ii. THL hosts the Finnish National Biobank (www.nationalbiobanks.fi) including well-characterized and well-documented Finnish cohort studies (i.e. ATBC, FINRISK, Health2000, HSDS, NFBC, Finnish Twin, Finnish Family studies) as well as international network studies such as GenomEUtwin, GEHA and MORGAM. THL/FIMM will bring expertise to DIA-EU-BBMRI from international leaders in molecular genetics, twin studies/epidemiology, bioinformatics and statistical genetics and contribute knowledge and experiences accumulated from the national biobanking and international networking efforts. The groups involved have demonstrated competence in large scale molecular epidemiology projects on complex diseases in the national, Nordic and European context. THL/FIMM participates in many international collaborative projects, including ENGAGE(FP7), BBMRI-Preparatory Phase(FP7), Gen2Phen(FP7), GEHA(FP6), PHOEBE(FP6), NeuroproMiSe(FP6), SGENE(FP6), PaGE-OM consortium, SynSys (FP7,under negotiation).
For the purpose of DIA-EU-BBMRI, the following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Dr. Markus Perola	THL/FIMM	Biobanking, genetics for complex diseases
Prof. Leena Peltonen	FIMM/THL	Human genetics, population genetics
Dr. Samuli Ripatti	FIMM/THL	Statistical genetics
Dr. Juha Muilu	FIMM/THL	Bioinformatics
Dr. Helena Kääriäinen	THL	Ethical & Societal issues
Prof Veikko Salomaa	THL	Epidemiologist
Prof Arpo Aromaa	THL	Epidemiologist

Relevant publications:

	Authors, Title, Year, Name journal
1	S Sabatti et al., Genome-wide association analysis of metabolic traits in a birth cohort from a founder population. 2009. Nat Genet
2	Aulchenko et al, Loci influencing lipid levels and coronary heart disease risk in 16 European population cohorts. 2009. Nat Genet
3	Thorisson G A et al., Genotype-Phenotype Databases: Challenges and Solutions For The Post-Genomic Era, 2009, Nature Review Genetics
4	Newton-Cheh et al., Genome-wide association study identifies eight loci associated with blood pressure. 2009. Nat Genet [Epub ahead of print]
5	Soranzo et al, A genome-wide meta-analysis identifies 22 loci associated with eight hematological parameters in the HaemGen consortium, 2009. Nat Genet [Epub ahead of print].

Partner 8 – International Prevention Research Institute - IPRI, Lyons France – Lead contact: Markus Pasterk

The International Prevention Research Institute (iPRI) was founded by a group of epidemiologists and biostatisticians highly experienced in the field of chronic disease prevention. iPRI is a new concept in biomedical research combining a thorough, high-level, academic approach coupled with a practical focus on providing clear information about evidence-based individual and population-based prevention strategies. It serves as an independent authoritative source of advice on critical risk issues and as a high-level training centre in all aspects of Prevention Research. All senior partners hold academic positions at different Universities around the world.
iPRI has established a training policy for internal and external trainees through the research projects involved. iPRI staff are internationally known scientists with academic affiliations; iPRI has an academic partnership with the University of Dundee ("iPRI-Dundee") which allows the supervision of PhD students involved in iPRI studies; iPRI-Dundee is holding an annual Summer School aimed at participants from low- income and lower-middle income countries on Epidemiology and Global Health; iPRI is engaging itself in the preparation and management of training courses around the world.

The following principal scientific /technical personnel are involved:

Name	Affiliation	Expertise
Markus Pasterk	COO, IPRI	Research Project Management, International politics of biobanking
Peter Boyle	Prof, President of IPRI	Epidemiology, Biostatistics, Research Management
Paolo Boffetta	Prof, Vice President Research of IPRI	Epidemiology, Biobanking, internat. large cohorts; course management
Philippe Autier	Research Director at IPRI	Clinical epidemiology, health technology assessment, screening

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Hainaut P, Betsou F, Bledsoe M, Burton P, Deschênes M, Fortier I, Hewitt R, Pasterk M, Riegman P, van Ommen GJ, Vaught J, Zatloukal K. Evidence-based standards for biobanking: the foundation of biomarker translational research for tomorrow's personalized medicine. 2009; Nature Biotech submitted
2	Yuille M, van Ommen GJ, Bréchot C, Cambon-Thomsen A, Dagher G, Landegren U, Litton JE, Pasterk M, Peltonen L, Taussig M, Wichmann HE, Zatloukal K. Biobanking for Europe. Brief Bioinform. 2008 Jan;9(1):14-24.
3	Bartsch G, Horninger W, Klocker H, Pelzer A, Bektic J, Oberaigner W, Schennach H, Schafer G, Frauscher F, Boniol M, Severi G, Robertson C and Boyle P on behalf of the Tyrol Prostate Cancer Screening Group. Tyrol Prostate Cancer Demonstration Project: Early Detection, Treatment, Outcome, Incidence and Mortality. BJU Int. 2008 Apr;101(7):809-16.
4	Pasterk MG. Genome research in Austria--a program of the future. Pharmacogenomics. 2002 Nov;3(6):829-33.
5	Boffetta P, Clark S, Shen M, Gislefoss R, Peto R, Andersen A. Serum cotinine level as predictor of lung cancer risk. Cancer Epidemiol Biomarkers Prev 2006;15:1184-8.

Partner 9 – The University of Manchester (UniMAN) – Lead contact: Dr. Bill Ollier

The University of Manchester is a major research university and is currently ranked 4oth in the world and 6th within Europe. It currently receives in excess of £250 million in research income each year. It was ranked as the 4th highest UK university in the last national research assessment exercise(RAE). The University of Manchester is the host University for The UK Biobank project which represents the largest longitudinal biobank study of its kind. The Centre for Integrated Genomic Medical Research (CIGMR) is a genomic resource centre where large scale genetic epidemiology and biobanking projects are conducted . Many national and international projects investigating the genetic and environmental bases of common complex disorders are currently underway. CIGMR has been an active participant in the FP7 BBMRI project.

Professor Bill Ollier has a long international track record for his work in large scale genetic epidemiology projects and has contributed extensively to previous European projects relating to biobanking and sample management. He is currently a Board member for UK Biobank. His particular interests are in harmonization, quality measures, and education in transnational research structure including biological sample management networks. He is currently a co PI on the UK DNA Banking Network project which manages and distributes large numbers of samples for collaborative research.

Dr Martin Yuille is regarded as an international leader in the development of sample access models and is currently associate coordinator for the FP7 BBMRI infrastructure scoping project. He is also a co PI for the UK DNA Banking Network. He is internationally recognized for his expertise in Biological sample management.

The following principal scientific and/or technical personnel are involved:

Name	Affiliation	Expertise
William Ollier	The University of Manchester	Complex genetic analysis and biobanking
Martin Yuille	The University of Manchester	Biobanking and sample resource management
Tim Peakman	UK Biobank/The University of Manchester	Biobanking and sample resource management

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Ollier W, Sprosen T, Peakman T. UK Biobank: from concept to reality. Pharmacogenomics 2005; 6(6): 639-646.

2	European Science Foundation Expert Group on Population Surveys and Biobanking. Population Surveys and Biobanking. ESF: Science Policy Briefing 2008; 32: 1-10.
3	Brown J, Donev AN, Aslanidis C, Bracegirdle P, Dixon KP, Foedinger M, Gwilliam R, Hardy M, Illig T, Ke X, Krinka D, Lagerberg C, Laiho P, Lewis DH, McArdle W, Jones RW, Patton S, Ring SM, Schmitz G, Stevens H, Tybring G, Wichmann HE, Ollier WE, Yuille MA. Observational study on variability between biobanks in the estimation of DNA concentration. BMC Res Notes 2009; 2(1): 208; Epub ahead of print.
4	Yuille M, Dixon K, Platt A, Pullum S, Lewis D, Hall A, Ollier W. The UK DNA banking network: a "fair access" biobank. Cell Tissue Bank 2009; Epub ahead of print.
5	Amoli MM, Carthy D, Platt H, Ollier WER. EBV Immortalization of human B lymphocytes separated from small volumes of cryo-preserved whole blood. Int J Epidemiol 2008; 37(suppl_1): i41-i45.

Partner 10 – University of Leicester, UK (ULEIC) – PIs: Profs. P. Burton & A.J. Brookes

This is one of few British universities in the world's top 200, (15th out of 117 in the UK), and is a member of the '1994 Group' of research intensive universities. Annual research income exceeds£41.5M, including >£12M of EC awards in FP6 and >€15 million in FP7. The Departments of Genetics and Health Sciences, which are highly recognized internationally and which together control >£15.5M of research funds, will participate in the DIA-EU-BBMRI bid.

Prof. Paul Burton is Head of the Genetic Epidemiology group, which has strengths in the genetics and environmental determinants of complex diseases and in the development of statistical and epidemiological methodologies for their study. Work in his research group focuses on: design and harmonization of biobanks, large scale pooling projects in genetic epidemiology, methods for the analysis of family-based and longitudinal studies, and causal modeling. He is Chair of the steering committee of P3G, the Access Committee that oversees most UK birth cohorts, and the Study Design Expert Group at Wellcome Trust. Dr Nuala Sheehan is Reader in Genetic Statistics. Her research program focuses primarily on causal modeling, Mendelian Randomization, graphical modeling and the identification of relatives from genomic data. Dr Martin Tobin is MRC Clinician Scientist in Genetic Epidemiology. His research has a focus on clinical genetic epidemiology – cardiovascular and respiratory science – and he has extensive experience and theoretical knowledge in the analysis of genome wide association studies (GWAS). He has played a lead role in two successful large scale consortium-based GWASs.

Prof. Anthony Brookes Heads a Bioinformatics and Genomics group (9 postdocs, 2 students, 2 technicians), which has strengths in novel technology development for human genome variation data generation and data management. He serves on the HUGO Council, is a Founding Board Member of the Human Genome Variation Society (HGVS), is communicating editor for the journal Human Mutation, and has published 135 peer-reviewed scientific articles. His team runs the HGVbaseG2P association database, and he coordinates GEN2PHEN - a EUR12M FP7 genotype-phenotype database federation project. He is also a WP leader in the FP7 READNA project which seeks new breakthroughs in DNA sequencing and analysis methods. His post-doc members run independent aspects of the group's overall program of work, and raise their own funds to do so.

The following principal scientific and/or technical personnel are involved:

Name	*Institution*	*Expertise*
Paul Burton	ULEIC	Epidemiology
Anthony Brookes	ULEIC	Genetics Bioinformatics
Susan Atkinson	ULEIC	Biobank harmonization
Robert Hastings	ULEIC	Genetics Postdoc programmer
Robert Free	ULEIC	Genetics Postdoc programmer
Gudmundur Thorisson	ULEIC	Genetics Postdoc programmer
Sirisha Gollapudi	ULEIC	Genetics Postdoc programmer

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	G.A.Thorisson, J.Muilu, A.J.Brookes. Genotype-Phenotype Databases: Challenges and Solutions For The Post-Genomic Era. Nature Reviews Genetics (2009) 10, 9-18.
2	Patrinos GP, Brookes AJ. DNA, Diseases, and Databases: Disastrously Deficient. Trends Genetics 2005; 21: 333-8.
3	Burton PR, Hansell AL, Fortier I, Manolio TA, Khoury MJ, Little J, Elliot P. Size matters: just how big is BIG?: Quantifying realistic sample size requirements for human genome epidemiology. International Journal of Epidemiology 2009;38:263-273
4	Palmer TM, Thompson JR, Tobin MD, Sheehan NA, Burton PR. Adjusting for bias and unmeasured confounding in Mendelian randomization studies with binary responses. International Journal of

Epidemiology, 2008:37:1161–1168

Partner 11 – Karolinska Institutet, Stockholm - Sweden – Lead contact: Prof. Jan-Eric Litton

Litton group**:** Jan-Eric Litton is Professor of Biomedical Computing at Karolinska Institutet. Today Litton is leading an infrastructure group in the pan-European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI). Litton is and one of two leaders in bbmri.se and sitting in the Research Council Committee for Biobanks in Sweden (BISC). The Twin-Net has been developed by the Litton group at KI in collaboration with the Department of Molecular Medicine at the University of Helsinki The Twin-Net, a part of the EU project GenomEUtwin system, allows effortless data exchange and pooling of analyses from 600,000 twin pairs from 7 European countries and Australia. It provides a transparent virtual view of data stored in various computer systems and databases.

Jan-Eric is co-director and for the Swedish LifeGene initiative, a prospective cohort study with 500.00 individuals - www.lifegene.se. He is also heading the development of e-epidemiology by using Internet, cell-phones, digital paper and digital TV for collecting epidemiology data. Litton has also made major contributions to the current knowledge in Positron Emission Tomography (PET).

Dillner group: Prof. Joakim Dillner is professor of infectious disease epidemiology of the Karolinska Institute, Stockholm, Sweden and Principal Investigator of the WHO HPV LabNet Global Reference Laboratory, Malmö, Sweden. He is coordinator of the Swedish National Biobanking Program bbmri.se, chairman of the Nordic Biological Specimen Banks working group on Cancer Causes & Control and the Southern Sweden Maternity Biobank. He is also Work Package leader for the WP on biobanks of the FP7 ERA-NET EUROCOURSE on registries & biobanks (www.eurocourse.org). He has previously coordinated several EU networks, most recently the FP6 Network of Excellence on registries & biobanks Cancer Control using Population-based Registries & Biobanks (CCPRB;www.cancerbiobank.org). He has published about 250 papers in international peer-reviewed journals on the papilloma viruses and on the science of biobanking.

We will be part of WP 1.1 (Litton), lead WP 2.1 (Litton, Fransson) and part of WP 2.2 (Dillner). We has also been actively involved in P3G (Litton IWG2 leader 2005-2008) and Phoebe (Litton WP leader).

The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Jan-Eric Litton	Professor of Biomedical Computing, MEB, Karolinska Institutet	e-Epidemiology, Biobanking, informatics, computer science
Joakim Dillner	Professor of infection disease epidemiology, Karolinska Institutet	Epidemiology, Infection disease, Biobanking and Health registries
Martin Fransson	M. Sc., Applied Physics and Electrical Engineering, Licentiate of Engineering. MEB, Karolinska Institutet	Biobanking, project planning, mathematical modeling

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Muilu J, Peltonen L, **Litton JE**. The federated database--a basis for biobank-based post-genome studies, integrating phenome and genome data from 600,000 twin pairs in Europe. Eur J Hum Genet. 2007 Jul;15(7):718-23.
2	Yuille M, van Ommen G-J, Bréchot C, Cambon-Thomsen A, Bagher G, Landegren U, **Litton J-E**, Pasterk M, Peltonen L, Taussig M, Wichmann H-E, Zatloukal K. Biobanking for Europe. Brief Bioinform. 2008 Jan;9(1):14-24.
3	Ölund G, Lindqvist P, **Litton J-E**. BIMS: An information management system for biobanking in the 21st century. IBM Systems Journal. 2007;46(1):171-82.
4	Ivarsson, M.I., **Dillner, J**. and Carlson, J. Validity of maternal genotypes in DNA from archival pregnancy serum samples. *Clinical Chemistry*. **55**. 842-843. 2009.
5	**Dillner, J**., Rebolj, M., Birembaut, P., Petry, K-U., Szarewski, A., Munk, C., de Sanjose, S., Naucler, P., Lloveras, B., Kjaer, S., Cuzick, J., van Ballegooijen, M., Clavel, C. and Iftner, T. Long term predictive values of cytology and human papillomavirus testing in cervical cancer screening: joint European cohort study. *British Medical Journal*. 337:a1754. 2008.

Partner 12 – Helmholtz Center Munich, National Research Center for Environmental Health (HMGU) – Germany – Lead contact: Prof. H.-Erich Wichmann

The Helmholtz Center Munich, National Research Center for Environmental Health (HMGU), is a federally funded research center located in Neuherberg/Munich, Germany. Multidisciplinary research of the HMGU is focused on activities related to the protection of man and his environment as well as the utilization of scientific and technical knowledge to improve health care.

Prof. H.-Erich Wichmann is Director of the Institute of Epidemiology, HMGU, and holds the Chair of Epidemiology at Munich University. He has a long lasting expertise in environmental epidemiology and genetic epidemiology. He is responsible for several population based cohorts and disease related epidemiological studies and is PI of KORA. He participates in several EU projects (ENGAGE, MORGAM, CARDIOGENICS). He was a member of the steering committee, WP leader and national contact for Germany in the preparatory phase of BBMRI,

Prof. Thomas Meitinger is Head of the Institute for Human Genetics. He was member of the steering committee in the preparatory phase of BBMRI and a co-leader in the German rare disease network for mitochondrial disorders.

Associate Professor Thomas Illig is Head of the group "Molecular Epidemiology" of the HMGU. He has a longstanding experience in molecular and genetic epidemiology. He is in the advisory board of the federal government for metabolic diseases. One main focus is the molecular analysis of asthma, atopic eczema, cardiovascular diseases as well as of diabetes. He participates in EU-projects GABRIEL, ARTHEROREMO and NUTRIMENTHE.

Dr. Christian Gieger is a statistician leading the group of genetic epidemiology. He is involved in a large number of genome-wide association projects and made contributions to combine genomics and metabolomics.

The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Prof. H.-Erich Wichmann (Lead contact)	HMGU	Biobanking, environmental and genetic epidemiology, population studies, PI KORA
Prof. Thomas Meitinger	HMGU	Human genetics, biobanking
Assoc. Prof. Thomas Illig,	HMGU	Biobanking, molecular epidemiology, genomics, metabolomics
Dr. Christian Gieger	HMGU	genetic epidemiology, genomics, metabolomics

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Herbert A, Wichmann HE, Illig T et al. A common genetic variant is associated with adult and childhood obesity. Science. 2006 14;312(5771):279-83. (IF: 30.0)
2	Zeggini E,, Illig T et al. Meta-analysis of genome-wide association data and large-scale replication identifies additional susceptibility loci for type 2 diabetes. Nat Genet. 2008 May;40(5):638-45. (IF: 25.6)
3	Gieger C, Illig T, Wichmann HE et al. Genetics meets metabolomics: a genome-wide association study of metabolite profiles in human serum. PLoS Genet. 2008 Nov;4(11):e1000282. (IF: 10.9)
4	Aulchenko, YS, Gieger, C, Wichmann, HE, et al. Loci influencing lipid levels and coronary heart disease risk in 16 European population cohorts. Nat Genet 41(1), 47-55 (2009)
5	Pfeufer, A, Wichmann HE, Meitinger T et al.: Common variants at ten loci modulate the QT interval duration in the QTSCD Study. Nature Genetics 41(4), 407-414 (2009)

Partner 13 – Babraham Bioscience Technologies, Cambridge, UK (BBT) – Lead contact: Dr M Taussig

BBT is a commercial Enterprise with a staff of 24 and is a wholly-owned subsidiary of the Babraham Institute. BBT laboratories provide modern, fully fitted facilities together with access to comprehensive scientific and technical support services (mass spectrometry, confocal microscopy, bioinformatics, etc) at the Institute. BBT also manages a highly successful bioincubator and actively promotes collaborative development programmes and the creation of spinout companies. The Protein Technology Group (Head, Dr M Taussig) develops systems of antibody and protein production, such as ribosome display and protein array systems, on which BBT has obtained patents.

Role in BBMRI: Dr Mike Taussig will coordinate WP1.3 dealing with Molecular tools and technologies, jointly with Professor Ulf Landegren (UU). Dr Taussig has considerable experience of managing large scale European networking and research projects, having been management coordinator of the FP6 MolTools consortium, and currently coordinator of the ProteomeBinders FP6 Research Infrastructure Coordination Action. He is also joint WP4 coordinator in the preparatory phase of BBMRI, with responsibility for protein and antibody resources in Europe. BBT will provide the financial and administration services for management of WP1.3.
Key staff: Dr Mike Taussig is Head of the Protein Technology Group at BBT. As former head of the Babraham Institute Technology Research Group, his experience includes structure of antibodies, protein display methods, protein array design, cell free protein expression and X-ray crystallography. He is co-inventor of ribosome display technology and the PISA and DAPA methods for production of protein arrays. As noted above he has considerable experience of framework project coordination, both at the networking and research levels, and is developing through the ProteomeBinders project a plan for a European resource of binding molecules for analysis of the human proteome. **Dr Oda Stoevesandt** obtained her PhD from University of Tübingen (2006) on novel binder-based approaches for measuring protein-protein interactions by fluorescence cross correlation spectroscopy and peptide microarrays. She has been the administrator for the FP6 ProteomeBinders project for the last three years. **Dr Cheryl Smythe** is an experienced administrative assistant who has coordinated the European Science Foundation programme in function genomics.
The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Dr Mike Taussig	Head of the Protein Technology Group at BBT	structure of antibodies, protein display methods, protein arrays, cell free protein expression, X-ray crystallography
Dr Oda Stoevesandt	BBT	Project manager
Dr Cheryl Smythe	BBT	Project assistant

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Gloriam DE et al (2009) Report A community standard format for the representation of protein affinity reagents. *Mol. Cell Proteomics* (epub ahead of print)
2	Apweiler R et al. (2009) Approaching clinical proteomics: current state and future fields of application in fluid proteomics. *Clin Chem Lab Med.* 47:724-44
3	Taussig MJ et al. (2007) ProteomeBinders: Planning a European Resource of Affinity Reagents for Analysis of the Human Proteome. *Nature Methods* 4:13-17;
4	Stoevesandt, O. and Taussig, M.J. (2007) Affinity reagent resouces for human proteome detection - initiatives and perspectives. *Proteomics* 7: 2738-2750
5	He, M and Taussig MJ (2007) Eukaryotic ribosome display with in situ DNA recovery. *Nature Methods* 4:281-288

Partner 14 – Legal Pathways Institute for Health and Bio-Law

The Legal Pathways Institute for Health and Bio-Law is an independent legal research organisation. Its areas of expertise include health law, pharmaceutical law, data protection law, technology transfer and biomedical research law, both at the national and the international level. Its goal is to help the biomedical research community navigate the legal pathways that govern its cross border, multi-jurisdictional operations. To that end it has designed, developed and built for BBMRI a website containing a WIKI-platform for legal documents and instruments.
Legal Pathways will bring to the project its specific expertise on the legal aspects of cross border biobanking and biomedical database building, combining years of practical experience and academic analysis. LP's track record, its network of EU specialists and its technology driven approach seem particularly fit to roll out the WIKI Legal Platform across the EU and to perform the underlying work of identifying and addressing the legal issues associated with the innovative cross border research activities envisaged by the project.
For the purpose of BioSHaRE-EU, the following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
JA Bovenberg	Legal Pathways	Legal

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Bovenberg et al. Biobank Research: Reporting Results to Individual Participants, European Journal of Health Law 16 (2009) 229-247.

2	Bovenberg et al. Your Biobank, Your Doctor? The right to full disclosure of population biobank findings, Genomics, Society and Policy, 2009, Vol.5, No.1, pp.1-25
3	Bovenberg et al. Legal Pathways for Cross Border Research, European Journal of Human Genetics, January 2007.
4	Bovenberg et al., "Humane Biotechnologie en Recht", preadvies Nederlandse Juristen Vereniging 2009 (Kluwer 2009).
5	Bovenberg, Whose tissue is it Anyway? Nature Biotechnology, Vol 37, August 2005.

Partner 15 – The Norwegian Institute of Public Health (NIPH), Oslo Norway – Lead contact: Dr. Jennifer Harris

The mission of The Norwegian Institute of Public Health (NIPH) is to improve public health. It is a national centre for expert knowledge of epidemiology, infectious disease control, environmental medicine, forensic toxicology and research on drug abuse. The Division of Epidemiology at the Norwegian Institute of Public Health (NIPH) monitors the health of the population, much of this is through research on data collected and analyzed at the NIPH. It administrates large research and health registries and hosts the Norwegian Network of Human Research Biobanks and Health Studies: BioHealth Norway, which includes two major biobank facilities as national services. Scientific and other personnel within the department of epidemiology at NIPH work with the biobanks and associated projects, in collaboration with international networks in Europe and in the USA. Researchers from NIPH are highly involved in European biobanking initiatives including BBMRI, GenomEUtwin, PHOEBE, and ENGAGE.

The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Jennifer Harris	NIPH	Human Development, Genetic Epidemiology
Isabelle Budin Ljøsne	NIPH	Bioethics,
Camilla Stoltenberg	NIPH	Epidemiology, Genetic Epidemiology
Per Magnus	NIPH	Epidemiology, Genetic Epidemiology

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Gudbjartsson DF, Holm H, Gretarsdottir S, et al., A sequence variant in ZFHX3 on 16q22 associates with atrial fibrillation and ischemic stroke. Nat Genet. 2009. 41(8):876-8.
2	Kettunen J, Perola M, Martin NG, et al., Multicenter dizygotic twin cohort study confirms two linkage susceptibility loci for body mass index at 3q29 and 7q36 and identifies three further potential novel loci. 2009. Int J Obes. 33(11):1235-42.
3	Agurs-Collins T, Khoury MJ, Simon-Morton D, et al. Public health genomics: translating obesity genomics research into population health benefits. 2008. Obesity. 16 Suppl 3:S85-94.
4	Perola M, Sammalisto S, Hiekkalinna T, et al., GenomEUtwin Project. Combined genome scans for body stature in 6,602 European twins: evidence for common Caucasian loci. 2007. PLoS Genet.3(6):e97.
5	Magnus P, Irgens LM, Haug K, et al. Cohort profile: the Norwegian Mother and Child Cohort Study (MoBa). 2006. Int J Epidemiol.35(5):1146-50.

Partner 16 – Erasmus Medical Center Rotterdam (EMC), Austria – Lead contact: Dr. PHJ Riegman.

The Department of Pathology of the Erasmus MC, includes a team of pathologists, biomedical scientists, research technicians and managerial personnel who join forces to implement and improve high standards of diagnostic pathology and experimental research breast, brain, colon and urogenital cancers. It is located in the Josephine Nefkens Institute (JNI), the dedicated cancer research building of the Erasmus MC, the largest academic medical center in the Netherlands with over 10,000 people as personnel and 1200 beds. Since 1998, the Josephine Nefkens Institute (JNI) encompasses various research groups and departments from the Daniel den Hoed Cancer Center (DDHCC) and the EUR (merged in 1994 into the Erasmus MC) working on the molecular pathology of cancer. The JNI hosts more than 200 among scientists and clinicians from five different departments collaborating in a multi-disciplinary fashion.

Facilities: 4000 m2 of laboratories and research facilities, (Tissue bank specific: laser aided micro dissection (PALM), virtual microscopy (Hamamtsu Nanozoomer), automated tissue micro arrayer (Beecher ATA27)), Affymetrix platform, tissue biobank, cell culture, animal house, and flow-sorting facilities, together with fully operational genomics and proteomics appliances, and in vivo high-resolution imaging and microscopy.

Websites: www.erasmusmc.nl, www.tubafrost.org, www.eurobonet.org, www.pathobiology.eu.

Specific expertise related to the field: The Erasmus MC Tissue Bank has a wealth of knowledge regarding the pre-analytical phase of diagnostics and useful infrastructure that can be used for this project. EMC still leads the successful pioneering European biobanking project "The European Human Frozen Tumor Tissue Bank" or OECI-TuBaFrost, which was further developed in EuroBoNeT. Sustainability was found in the OECI. Extensive experience has been acquired with International Biobanking including standardisation, access rules, network database applications, ethics and law. The group has published high-impact journal articles regarding issues surrounding biobanking, including regarding regulatory and ethical issues on the exchange of residual tissue for research across Europe.
Other EU Projects: TuBaFrost (Coordinator), EuroBoNeT (WP leader), BBMRI (Participant), SPIDIA (WP leader)
The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Peter Riegman	Head Erasmus MC Tissue Bank	President ISBER International Society of Biological and Environmental Repositories Coordinator OECI-TuBaFrost, Chair OECI pathobiology group
Cornelia van Duijn	Professor in Molecular Biology	Epidemiology, Biobanking, Molecular biology, Genetics
Bas de Jong:	Assistant tissue resource manager	Molecular biology, Biobanking
Marcel Kap	PhD student	
Monique Oomen	Chief Engineer, Erasmus MC Tissue bank	Laboratory management, bio-analysis

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Peter H.J. Riegman, Manuel M. Morente, Fay Betsou, Pasquale de Blasio, Peter Geary and the Marble Arch International Working Group on Biobanking for Biomedical Research, Biobanking for better healthcare, Mol Oncol. 2008 Oct;2(3):213-222. Epub 2008 Jul 30. Review
2	Riegman PH, Dinjens WN, Oosterhuis JW. Biobanking for interdisciplinary clinical research. Pathobiology. 2007;74(4):239-44.
3	Mager SR, Oomen MH, et al. Standard operating procedure for the collection of fresh frozen tissue samples. Eur J Cancer. 2007 Mar;43(5):828-34
4	Morente MM, Mager R, et al.. TuBaFrost 2: Standardising tissue collection and quality control procedures for a European virtual frozen tissue bank network. Eur J Cancer. 2006 Nov;42(16):2684-2691
5	van Veen EB, Riegman PH, et al. TuBaFrost 3: regulatory and ethical issues on the exchange of residual tissue for research across Europe. Eur J Cancer. 2006 Nov;42(17):2914-2923

Partner 17 – deCODE genetics EHF, Iceland. Lead contact: Dr. Hákon Guðbjartsson

deCODE genetics has over 13 years of experience in genetics research and has been leading the discovery of genetic variants for many common diseases in past years. deCODE has extensive experience in molecular biology and provides genotyping services in the most high-throughput genotyping facility in the world. The company has a bio-bank, equipped with in-house developed sample robotics systems and LIMS software, managing millions of tissue samples from Icelandic study participants and from foreign research collaborators. Associated with the samples is a database with phenotypes and laboratory measurements from over hundred thousand participants, genealogy of the entire nation and 1M marker GW-SNP datasets for over 60 thousand research subjects.
deCODE has extensive experience in large-scale software development and has invested well over 500 hundred man-years in their development. This includes systems for electronic data-capture (Questor), cryptographic solutions for identity protection (IPS), LIMS software for our laboratory core-facilities, STS and SNP allele-calling signal-processing algorithms, statistical tools (NEMO, Allegro), high-throughput Sanger-sequencing software pipeline (SequenceMiner), a sophisticated genetic research workbench (DiseaseMiner) with tools for launching genetic and familial analysis on a HPC as well as a genome browser to visualize association results.

Furthermore, the company has developed highly advanced ad-hoc query and reporting module based on a proprietary Set Definition Language (SDL). In relation to the Icelandic Healthcare Database project, deCODE acquired significant expertise in inference control techniques and has experimented with various algorithms of that nature. For instance, we have developed a prototype of the SDL system with built in inference controls. Additionally, deCODE has processes and experience for developing software that complies with the requirements and standards for clinical trials and CLIA. For the past two years, the company has been marketing diagnostic products and consumer genetics through web-based systems, e.g. deCODEme.com and deCODEhealth.com.
deCODE has participated in numerous disease oriented EU projects and NIH projects. The company is also a active member in the preparation phase of BBMRI and a member in the GEN2PHEN project.
The following principal scientific /technical personnel are involved:

Name	*Affiliation*	*Expertise*
Hákon Guðbjartsson PhD	VP Informatics	Bioinformatics, cryptography, data-warehousing, softw.
Vilmundur Pálmason	Software engineer	Query-language compilers, Java & Ruby&Rails develop.
Guðmundur Fr. Georgsson	Software engineer	LIMS, encryption software, Java development
Guðbjörn F. Jónsson	Mathematician	Statistics, numeric computation and Java development

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	US7152073B2: A method and a system for defining sets by querying relational data using a Set Definition Language", H. Gudbjartsson, V. Pálmason, T. S. Arnarson, P. Rovensky, Dec. 19th, 2006.
2	US20020027519A1: Automatic identity protection system with remote third party monitoring, H. Gudbjartsson, S. Karlsson, S. Thormar, Oct. 4, 2001. Assignee deCODE Genetics.
3	US10/057,314: Inference control method in a data cube, A. S. Egilsson and H. Gudbjartsson, January 25th, 2002
4	US10/316,986 Indexing, rewriting and efficient querying of relations referencing semistructured data, A. S. Egilsson and H. Gudbjartsson, December 10th, 2002
5	J. Gulcher, K. Kristjansson, H. Gudbjartsson, K. Stefansson, "Protection of privacy by third-party encryption in genetic researc in Iceland", Euro. Journ. Hum. Genetics 8, 739-742 (2000)
6	B. Palsson, F. Palsson, M. Perlin, H. Gudbjartsson, K. Stefansson, J. Gulcher, "Using Quality Measures to Facilitate Allele Calling in High-Throughput Genotyping", Genome Research 9, 1002-1012 (1999)

Partner 18 – Life Science Governance Institute (LSG), Vienna. Lead contact: Professor Herbert Gottweis

The Life-Science-Governance-Institute researches central topics of contemporary life science governance, and develops solutions for good life science governance. It has been a partner in several FP EU projects, such as BBRMI (FP 7), REMEDI (Regenerative Medicine in Europe, FP 7), and TRANSNEURO (Neural Transplantation in Patients with Parkinson's Disease, FP 7). A special focus of LSGI is the study of the public perception of biomedicine.
Herbert Gottweis, born 1958, is professor at the Department of Political Sciences, University of Vienna since 1998. He also directs the Life Science Governance Institute in Vienna, an interdisciplinary research institutes working on the interface between life sciences and governance. He gained his Ph.D. from the University of Vienna (1984), was a visiting graduate student at the University of Rochester (1983/83), Assistant and Lecturer at the political science department, University of Salzburg (1985-1997), visiting research fellow (supported by a FWF Erwin Schrödinger Stipend) at the Centre of European Studies, Harvard University (1989/90), visiting research fellow (supported by the Andrew Mellon Foundation) at MIT's program in Science, Technology, and Society (1992/93), assistant professor at the Department of Science and Technology Studies, Cornell University (1993-95), visiting professor, Department of Social Studies, Hong Kong University of Science and Technology (1997) and visiting Professor at the Australian School of Environmental Studies, Griffith University (2004). Since 2005 he is also vice-president of the Austrian Research Fund (FWF).
Gottweis was the coordinator of the PAGANINI ("Participatory Governance and Institutional Innovation") project (2004-2007) funded as a STREP under the 6th EU Framework program and he also is partner in two other 6th EU Framework programme projects (BIONET, a China-EU network on ethical governance in bio-medical research (2006-2009) and GENBanC (2006-2009), a project on biobank governance. Under the 7th EU Framework program Gottweis is partner in REMDIE (Regenerative medicine in Europe: emerging needs and challenges in a global context) and in BBMRI (Biobank and Biomolecular Resources Initiative), a coordination action of biobank projects in Europe which he advises on ethical governance issues.
The following principal scientific and/or technical personnel are involved:

Name	Affiliation	Expertise
Herbert Gottweis	Life Science Governance Institute (LSG)	life science governance

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Prainsack, Barbara; Reardon, Jenny; Lunshof, Jannine; Gottweis, Herbert; Hindmarsh, Richard; Naue, Ursula (2008) Personal Genomics (PG) Services and the Post-Genomic Condition, Nature, 454, Nov 6, 34-35.
2	Gottweis Herbert (2008), Participation and the New Governance of Life, Biosocieties, 3, 265-285.
3	Gottweis Herbert & Minger Stephen, (2008): "iPS Cells and the Politics of Promise", Nature Biotechnology, 26, 271-272.
4	Gottweis Herbert & Petersen Alan (eds., 2008): Biobanks: Comparative Governance. London: Routledge.
5	Gottweis Herbert & Zatloukal Kurt (2007): "Biobank Governance: Trends and Perspectices", Pathobiology, 74, 206-211.

Partner 19 – UTARTU - Estonian Genome Project, University of Tartu, Tartu, Estonia. Lead contact - Prof. Andres Metspalu

The Estonian Genome Project (EGP) of University of Tartu is a research institute reorganized from the Estonian Genome Project Foundation in 01.04.2007. The Estonian Genome Project of University of Tartu carries on the goal of Estonian Genome Project to create a database (biobank) of health, genealogy and genome data and open of the resources to European Research Area. The legal framework for the activities of the EGP consists of the Constitution of the Republic of Estonia, the Human Genes Research Act (HGRA), the Personal Data Protection Act, the Databases Act and the Council of Europe Convention on Human Rights and Biomedicine. All the acts can be found from our website www.geenivaramu.ee. EGP is one of the first European population based biobanks and it is projected to collect c.a. 5% of adult population which is 50 000 samples by the end of 2010. There are currently (December 2009) ~40 000 subjects in the Estonian Biobank all with recorded health status plus DNA, plasma and WBC stored in liquid N2. The database will make it possible to carry out research both in Estonia and outside to find links between genes, environmental factors, lifestyles and common diseases (cancer, diabetes, depression, cardio-vascular diseases, etc). EGP has already existent cooperation within biobank consortiums P3G and ESFRI BBMRI. EGP is involved as a partner in 2 EU FP6 projects and 4 FP7 projects (ENGAGE, BBMRI, EUROCOURSE and OPENGENE) and the samples are used in many international collaboration projects (Sweden, Canada, FP projects EUCLOCK and LIFESPAN). EGP received an ISO 9001:2000 certificate in 2003 and has successfully renewed it. EGP has laboratory for DNA research, IT unit and data (health information and biological samples) collection unit. There are 22 employees in EGP at the moment.

The following principal scientific and/or technical personnel are involved:

Name	Affiliation	Expertise
Andres Metspalu, MD, PhD	UTARTU	human genetics, biobanks, microarrays, molecular diagnostics
Maido Remm, PhD	UTARTU	genetic analysis, bioinformatics
Eduard Maron, MD, PhD	UTARTU	neuropsychiatric diseases, phenotyping, epidemiology, imaging, animal models
Krista Fisher, PhD ethics, data protection,	UTARTU	biostatistics
Helene Alavere, MD, MSc	UTARTU	phenotyping, biobanks, epidemiology
Aime Keis, MD	UTARTU	ethics, data protection, biobank ethics, bioethics
Tõnu Esko, MSc	UTARTU	statistical analysis of complex phenotypes, WG analysis, bioinformatics

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Nikopensius T, Ambrozaitytė L, Ludwig KU, et al. Replication of novel susceptibility locus for nonsyndromic cleft lip with or without cleft palate on chromosome 8q24 in Estonian and Lithuanian patients. Am J Med Genet A. 2009 Oct 16;149A(11):2551-2553.
2	M. Kuningas, L. May, R. Tamm, D. van Bodegom, et al. Selection for Genetic Variation Inducing Pro-Inflammatory Responses under Adverse Environmental Conditions in a Ghanaian Population. PLoS One. 2009 Nov 11;4(11):e7795.
3	Maria Teresa Landi, Nilanjan Chatterjee, Kai Yu, Lynn R. Goldin, et al. A Genome-wide Association Study of Lung Cancer Identifies a Region of Chromosome 5p15 Associated with Risk for Adenocarcinoma. The

	American Journal of Human Genetics 85, 1–13, November 13, 2009
4	Mari Nelis, Tõnu Esko, Reedik Mägi et al. Genetic Structure of Europeans: a view from the North-East. PlosOne 2009, http://dx.plos.org/10.1371/journal.pone.0005472
5	Khrunin A, Mihailov E, Nikopensius T et al. Analysis of Allele and Haplotype Diversity Across 25 Genomic Regions in Three Eastern European Populations. Hum Hered 2009;68:35-44 (DOI: 10.1159/000210447)

Partner 20 – University of Salamanca, Spain (USAL). Lead contact: Dr. Alberto Orfao de Matos

The Spanish National DNA Bank (University of Salamanca), hereafter named BNADN is an S&T platform supported by Genoma España Foundation, whose main goal is to support genetic/genomic research by providing high-quality DNA human samples and associated data for individual researchers, research networks, consortia and institutions, assuring their rational and effective, ethical, legal and scientific use. In addition to these collections, the BNADN also provides other services which include: DNA extraction, cell immortalization, education and consultancy on biobanking. For these aims, robotic technologies for DNA extraction and liquid sample handling are available together with biosecurity-safe level III laboratory facility for cell immortalization and high throughput cell separation facility (Flow Cytometry and MACS cell sorters). Since its creation in March 2004 till now, the BNADN has collected more than 27,000 samples from an identical number of individuals. Since 2006, its structure is formed by five different nodes (central coordinating node plus four nodes on prevalent diseases: cardiovascular, neuropsychiatric, metabolic and oncological diseases). The current nodal structure involves signed collaborations with more than sixty different institutions, including twenty nine regional transfusion centres, thirty six hospital and research centres, two private foundations and two major national scientific medical associations. The collected samples are structured into healthy controls (n= 3370; including 110 individuals with > 90 years), population-based cohorts (n=3488), and patients with oncological (n=3904), neuropsychiatric (n=1334), metabolic (n=3270), cardiovascular (n=2117), immunologically mediated chronic inflammatory disorders (n=7157), as well as other rheumatologic disorders (n=2131) and some rare diseases (n=331). Prof. Alberto Orfao is the Scientific Director of the Spanish National DNA Bank since its creation and he is also the Director of the General Cytometry Service at the University of Salamanca, as well as a principal investigator at the Cancer Research Centre of Salamanca. His research activities focus on immunology and cancer, particularly on hematological malignancies (leukemia's, lymphomas and multiple myeloma) and mainly on the study of the biological (phenotypical, genetic and functional) characteristics of the tumour clone and its effects on the evolution of the disease, as well as the treatment monitoring through the investigation of minimal residual disease. With all other members of the BNADN provides strong expertise in biobanking (clinical samples), advanced flow cytometry (sorting of pure cell populations and immunophenotyping) and extensive experience in coordination of National and European networks.

The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Alberto Orfao, MD, PhD	BNADN	Biobanking, Flow Cytometry, Hematology
Enrique de Álava, MD, PhD	BNADN	Cancer, Pathology, Biobanking
Andrés García-Montero, PhD	BNADN	Biobanking, Molecular Biology
María Almeida, PhD	BNADN	Biobanking, Flow Cytometry
Rosa Pinto, PhD	BNADN	Molecular Biology, Quality Control

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Nieto WG, et al. Primary Health Care Group of Salamanca for the Study of MBL. Increased frequency (12%) of circulating chronic lymphocytic leukemia-like B-cell clones in healthy subjects using a highly sensitive multicolor flow cytometry approach. Blood. 2009 Jul 2;114(1):33-7. Epub 2009 May 6.
2	Quijano S, et al. Spanish Group for the Study of CNS Disease in NHL. Identification of leptomeningeal disease in aggressive B-cell non-Hodgkin's lymphoma: improved sensitivity of flow cytometry. J Clin Oncol. 2009 Mar 20;27(9):1462-9. Epub 2009 Feb 17.
3	Pérez-Caro M, et al. Cancer induction by restriction of oncogene expression to the stem cell compartment. EMBO J. 2009 Jan 7;28(1):8-20. Epub 2008 Nov 27.
4	Rodriguez-Caballero A, et al. Expanded cells in monoclonal TCR{alpha}{beta}+/CD4+/NKa+/CD8-/+dim T-LGL lymphocytosis recognize hCMV antigens. Blood. 2008 Dec 1;112(12):4609-16. Epub 2008 Sep 2.
5	Quijano S, et al. Association between the proliferative rate of neoplastic B cells, their maturation stage, and underlying cytogenetic abnormalities in B-cell chronic lymphoproliferative disorders: analysis of a series of 432 patients. Blood. 2008 May 15;111(10):5130-41. Epub 2008 Mar 12.

Partner 21 – Technische Universität München (TUM) – Lead contact: Prof. Klaus A. Kuhn

Technische Universität München has earned high international reputation, which is apparent from research collaborations with more than 140 partner universities and its involvement in about 150 FP-6 and currently (November 2009) more than 70 FP-7 projects, 420 projects financed by the German Research Ministry, and in 17 special research programs (SFB) financed by the German Research Association (DFG).
Prof. Klaus A. Kuhn is Chair of Medical Informatics at TUM and Director of the Institute of Med. Biometry and Epidemiology at the University Medical Center "Klinikum Rechts der Isar" of TUM. He is a faculty member of both the medical and the computer science faculty. His institute has a strong focus on the design and realization of information systems for translational research, comprising information integration, IT for research systems and biobanks. The institute is involved in national projects funded by the Research Ministry and DFG, and it has actively participated in the preparatory phase of BBMRI. Prof. Kuhn is Vice President of the German Assoc. for Med. Informatics, Biometry, and Epidemiology, and he is a Fellow of the American College of Med. Informatics (ACMI). The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Klaus A. Kuhn	Technische Universität München (TUM)	medical informatics, biometry, epidemiology

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Feulner TM, et al. incl. Kuhn KA: Examination of the current top candidate genes for AD in a genome-wide association study. Mol Psychiatry 2009 Jan 6. Epub ahead of print, doi: 10.1038/mp.2008.141
2	Kuhn KA, Knoll A, Mewes HW et al: Informatics and medicine--from molecules to populations. Methods Inf Med 2008; 47(4):283-95
3	Blaser R, et al. incl. Kuhn KA: Improving pathway compliance and clinical performance by using information technology. Int J Med Inf 2007;76(2-3): 151-6
4	Kuhn KA, Guise DA, Lapao L, Wurst SHR: Expanding the Scope of Health Information Systems From Hospitals to Regional Networks, to National Infrastructures and Beyond. Meth Inf Med 2007; 46(4):500-502
5	Lenz R, Beyer M, Kuhn KA: Semantic integration in healthcare networks. Int J Med Inf 2007;76 (2-3): 201-7
6	Lenz R, Kuhn KA: Towards a continuous evolution and adaptation of information systems in healthcare. Int J Med Inf. 2004; 73: 75-89

Partner 22 – Uppsala University (UU), Sweden, Lead contact Prof. Ulf Landegren

Uppsala University (www.uu.se) is one of the leading comprehensive research universities in Sweden. Research is strong in many fields including biology, biomedicine and computer science. The University trains 40,000 undergraduate students and 2,500 graduate students, employing 3,800 teachers/researchers and 500 professors. It has a strong tradition for development of technologies for biological analyses. The research in this project will be conducted at the Department of Genetics and Pathology, which is located at the Rudbeck Laboratory, a translational research center hosting activities ranging from fundamental research to clinical routine in genomics, proteomics, and pathology. The research group involved in this project is actively developing enabling technologies for biomolecular analyses. Some of the earlier technologies have been licensed by companies such as Applied Biosystems, DuPont, Affymetrix, General Electric Healthcare, and the lab has also spun out several companies: Olink Bioscience (www.olink.com), Olink Genomics (www.olinkgenomics.com), and Q-linea (www.qlinea.com). Website: http://www.genpat.uu.se/en/node399
UU will make inventories of available technologies within the European Union and front-line research leading to future technologies for biobank analysis. The scope will include DNA technologies, protein technologies, binding reagents for their detection (e.g. antibodies) etc. Academic research will be included as well as industrial research and service provides. A public database will be established in which reagent resources and technologies will be stored.
The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Professor Ulf Landegren	Head of the Centre for Advanced Molecular Analysis	Molecular and micromechanical tools for high-precision analysis of genes and proteins. Oligonucleotide ligation assay (OLA), padlock probes for parallel or localized genetic analyses, and the proximity ligation technique for highly specific protein analyses

		High-throughput analyses of genes, transcripts, and proteins, and for detection of the location of single or interacting molecules in individual cells and clinical tissue

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Nilsson et al. (1994). Padlock probes: circularizing oligonucleotides for localized DNA detection. Science 265: 2085-2088.
2	Fredriksson et al. (2002). Protein detection using proximity-dependent DNA ligation assays. Nature Biotechnology 20: 473-477.
3	Gullberg et al. (2004). Cytokine detection by antibody-based proximity ligation. PNAS USA 101: 8420-8424.
4	Söderberg et al. (2006). Direct observation in situ of individual endogenous protein complexes. Nature Methods 3: 995-1000.
5	Schallmeiner et al. (2007). Sensitive protein detection via triple-binder proximity ligation assays. Nature Methods 4: 135-138 (2007).

Partner 23 – SLU, Uppsala, Sweden, Lead contact Dr. Erik Bongcam-Rudloff

The Swedish University of Agricultural Sciences (SLU www.slu.se) is the one of the two universities which founded the Linnaeus Centre for Bioinformatics (LCB). SLU-LCB undertakes high quality, cutting edge research ranging from microbial and mammalian genomics via computational functional genomics to molecular evolution. The main research disciplines such as Biology, Computer Sciences, and Mathematics are combined with bioinformatics to form a unique research platform.

The SLU-also manages the Swedish EMBnet node. EMBnet is a network of collaborating bioinformatics institutions in Europe and the rest of the world. EMBnet, one of the first, largest and still growing network of organizations giving bioinformatics oriented services. EMBnet was initiated by the EMBL, (www.embl.org), Heidelberg Germany in 1988 (www.embnet.org).

Our group will be responsible for the IT and bioinformatics work related to the creation of a web portal for biomolecular resources in WP1.3. The group will also coordinate the collection of methods and protocols and the design and implement of the molecular methods database "MolMeth". The group will also provide computer resources for the maintenance of the web portal and the "MolMeth" database. The group has extensive expertise in bioinformatics and, with EMBnet and the EMBRACE FP6 NoE, has pioneered the use of databases and web tools technologies for life sciences and is in the process of building the necessary know-how to tackle post-genomics new challenges in modern biosciences, such as Next Generation Sequencing platforms. See: www.nextgenerationsequencing.org.

Erik Bongcam-Rudloff is Associate Professor of Bioinformatics at the Linnaeus Centre for Bioinformatics, SLU, Uppsala, Sweden. He was the chairman of EMBnet 2003-09 (www.embnet.org) and he is a board member of EMBRACE (www.embracegrid.info), Eu-roKup (www.eurokup.org), HealtGrid (www.healthgrid.org), Uppmax (www.uppmax,uu,se), a WP4 member in BBMRI (www.bbmri-WP4.org) and a member of WP9 and 10 in ELIXIR (www.elixir-europe.org).

Profiles of individuals undertaking the work

Name	*Affiliation*	*Expertise*
Erik Bongcam-Rudloff	Associate Professor, SLU	Bioinformatics
Hans-Henrik Fuxelius	Post Doc, mathematician, SLU	Bioinformatics, phylogeny, database technologies.
Martin Norling	Civil Engineer in Bioinformatics, SLU	bioinformatics, programming, LIMS

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1.	David E. Gloriam, Sandra Orchard, Daniela Bertinetti, et. Al.. A community standard format for the representation of protein affinity reagents. Molecular and Cellular Proteomics. August 2009.
2.	Antonia Vlahou, Guenter Allmaier, Teresa Attwood, **et. al** , on behalf of EuroKUP "Report on the Second Combined Working Group and Management Committee Meeting of EuroKUP (Urine and Kidney Proteomics Cost Action)" Proteomics. Clinical Applications. August 2009. doi: 10.1002/prca.200900087
3.	Alvaro Martinez Barrio, Oskar Eriksson, Jitendra Badhai, et al. Targeted Resequencing and Analysis of the Diamond-Blackfan Anaemia Disease Locus RPS19 reveal considerable individual variation and novel regulatory modules. 2009 PlosOne, PLoS ONE 4(7): e6172. doi:10.1371/journal.pone.0006172

4. Jean SALZEMANN, Heinz STOCKINGER, Alvaro MARTINEZ BARRIO, Et Al.. Programmatic Access to Web Services: Connectivity and Interoperability for the European Life Sciences Community. Submitted

Partner 24 – Irish Platform for Patients' Organisations, Science and Industry (IPPOSI) - Lead contact: Derick Mitchell, PhD

IPPOSI is a unique partnership of Patient Groups/Charities, Science and Industry on the island of Ireland. As a patient led partnership, the platform provides a structured way of facilitating interaction between the three key membership groups (patients' organisations, scientists and industry (and where possible with State Agencies) on policy, legislation and regulation around the development of new medicines, products, devices and diagnostics for unmet medical needs in Ireland.

IPPOSI has been actively involved as partner in BBMRI-PP and is the administrative support to the BBMRI Stakeholders Forum. Michael Griffith, Chair of the BBMRI Stakeholders Forum is one of the original founding members of IPPOSI. Dr. Derick Mitchell, Executive Manager of the BBMRI Stakeholders Forum is based in IPPOSI and operates from the IPPOSI premises. IPPOSI and the BBMRI Stakeholders Forum are uniquely positioned to create a platform for informed debate and to demonstrate BBMRI's willingness to listen to stakeholders. IPPOSI will be expanding its definition and database of relevant BBMRI stakeholders throughout the remaining lifetime of the BBMRI-PP - participants will include patient groups, scientists, clinicians, representatives from different industries, ethical and legal institutions, politicians, as well as the media.

IPPOSI will organise the joint stakeholder/user conference planned in month 12. Within the BBMRI-PP, a Patient Working Group has been established, which aims to produce guidance and ensure effective Patient and Public Involvement in BBMRI and will also be consulted in designing appropriate training procedures for patient organisations on biobanking practices as part of Work package 1.4.

The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Mr. Michael Griffith	Chair, BBMRI Stakeholders Forum	Research Promotion, Extensive Networking, Organisation
Dr. Derick Mitchell	Executive Manager, BBMRI Stakeholders Forum	Molecular Medicine, Science Communication, Management of Multi-Stakeholder Forum
Ms. Eibhlin Mulroe	CEO, IPPOSI	Strategic Management, Communication and Networking

Partner 25 – HeLEX, University of Oxford - Lead contact: Dr. Jane Kaye

Dr. Jane Kaye is Wellcome Trust Fellow in Medical Law and Director of HeLEX,. Centre for Health, Law and Emerging Technologies at the, University of Oxford. She obtained her degrees from the Australian National University (BA); University of Melbourne (LLB); and University of Oxford (DPhil). She was admitted to practice as a solicitor/barrister by the Australian Capital Territory Supreme Court in 1997. She is a member of the Faculty of Law, University of Oxford and has taught both Regulation and Medical Law and Ethics courses at the University of Oxford. Her research in the area of law and genomics focuses on the development of innovative technologies and the legal issues of intellectual property rights, privacy, confidentiality, data protection and negligence, as well as the broader issues of the public interest, global governance and regulation. Her socio-legal research is based on issues that have implications for clinical and medical research practice. She is involved in a number of expert committees focusing on the issues surrounding biobanks within Europe and internationally.

Prior EU funding: European Commission Framework 5, Quality of Life grant 'Ethical, Legal and Social Aspects of Genetic Databases: A European Comparison (ELSAGEN)' with partners in Iceland, Sweden, Estonia and the UK, Contract number QLG6-CT-2001-00062, € 909,101.

HeLEX is a new interdisciplinary centre at the Department of Public Health, University of Oxford, researching law, policy and practice in the governance of health and emerging technologies. Current research focuses on genomics with an emphasis on global governance, privacy, data sharing frameworks, biobanks and translational research. It hosts a number of complementary research projects on aspects of the regulation, governance and management of databases and biobanks, including EnCoRe, which seeks to develop mechanisms for ensuring the appropriate levels of consent and the ability to revoke consent in research participants, and the Administrative Data Liaison Service which aids the communication and use of administrative data for research. Both provide access to a national and international network of researchers, and to industry partners through the EnCoRe including QinetiQ, HW Communications and Hewlett-Packard Laboratories.

University of Oxford: The first University to be established in the English-speaking world, and now comprising over 100 departments, and almost 5000 research active staff, the University of Oxford is a unique environment for strongly interdisciplinary research. Oxford has more world-leading academics (rated 4* in the 2008 national Research Assessment Exercise) than any other UK university, and the highest number of world-leading or

internationally excellent (4* or 3*) academics in the UK. In 2008 Oxford secured more research grants from the UK's Research Councils than any other institution and won more research income from external sponsors than any other UK university. Oxford's administrative infrastructure also provides excellent support in managing major grants and their outputs. All European research projects are supported by administrative staff and experienced personnel drawn from across the University of Oxford.
The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Dr. Jane Kaye	HeLEX	Law and ethics
Liam Curren	HeLEX	Law
Dr. Paula Boddington	HeLEX	Ethics
Naomi Hawkins	HeLEX	Law and ethics
Dr. Nadja Kaneloupoulou	HeLEX	Law and ethics

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Kaye J, Heeney C, Hawkins et al. Data-sharing in Genomics: changing Scientific Practice (2009) *Nature Reviews Genetics* 10:5, 331-335
2	Kaye J, Boddington P, de Vries J et al. Ethical Implications of the Use of Whole Genome Methods in Medical Research (Advance Online Publication: 2009) *European Journal of Human Genetics*. Advance online publication 4 November 2009; doi: 10.1038/ejhg.2009.191
3	P3G Consortium, Church G, Heeney C, Hawkins N, de Vries J, Paula Boddington. P, Kaye J., Bobrow M., Weir B., Public Access to Genome-Wide Data: Five Views on Balancing Research with Privacy and Protection. (2009) *PLoS Genetics* 5(10): e1000665 doi:10.1371/journal.pgen.1000665
4	Kaye J, Biobanking Networks: What are the Governance Challenges?, (In Press: 2009) in Kaye J & Stranger M, (Ed) *Principles and Practice in Biobank Governance* (Ashgate: Farnham)
5	Kaye J, Hawkins N, and Taylor J, Patents and Translational Research (2007) , *Genomics Nature Biotechnology* Vol. 25, No.7.

Partner 26 – University Klagenfurt UNI-KLu – Lead contact: Prof. Dr. Johann Eder

The University of Klagenfurt is a rather young Austrian University offering programs in Economics, business Administration, cultural sciences, humanities and last but not least informatics. The university is significantly expanding into technical areas under the topical umbrella of Ambient Intelligence. Currently there are 10 research groups in informatics/computer science with a clear orientation towards application oriented research. The group of Information Systems Engineering (Prof. Eder) has a good track record in research in two main areas: workflow systems and data warehousing / integration of heterogeneous databases. Within the 6th framework program of the European Union the group was partner in the Network of excellence INTEROP, and in the STREP-FET project "WS-Diamond". In the 7th framework programme the group is involved in the ESFRI project BBMRI. The group also secured grants in Austrian Genome Research program GEN-AU (GATIB-1 and GATIB-2) for establishing an IT-Architecture for biobanks and facilitate research based in biobanks. Key persons involved: Prof. Dr. Johann Eder is full professor for Information and Communication Systems at the University of Klagenfurt, Austria. Since 2005 is he is vice president of the Austrian Science Funds (FWF), heading the department of natural sciences and technology. The research interests of Prof. Eder are databases, information systems and knowledge engineering, in particular workflow systems and data warehousing techniques. He successfully directed several funded research projects in different areas, i.e. temporal data warehousing and data management in biobanks. He authored more than 100 peer-reviewed papers in international journals and conference proceedings. Dr. Christian Koncilia is researcher at the University of Klagenfurt, Austria. Before that he worked as managing consultant for a business intelligence vendor in Munich, Germany. His research interests are data warehousing, ontologies and evolution of information systems. He received his PhD in the area of temporal data warehousing and business intelligence. He authored several papers in international conference proceedings. The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Johann Eder	University of Klagenfurt	databases, information systems, data warehousing techniques
Christian Koncilia	University of Klagenfurt	data warehousing, ontologies, business information systems

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages

1	Martin Asslaber, Peter Abuja, Konrad Stark, et al.: The Genome Austria Tissue Bank (GATiB). 2007, Pathobiology.
2	Konrad Stark, Johann Eder, Kurt Zatloukal: Achieving k-anonymity in DataMarts used for gene expressions exploitation. 2007 J. Integrative Bioinformatics.
3	Johann Eder, Claus Dabringer, Michaela Schicho, Konrad Stark: Information Systems for Federated Biobanks. 2009. T. Large-Scale Data- and Knowledge-Centered Systems.
4	Konrad Stark, Jonas Schulte, Thorsten Hampel, Erich Schikuta, Kurt Zatloukal, Johann Eder: GATiB-CSCW, Medical Research Supported by a Service-Oriented Collaborative System.2008 LNCS (CAiSE).
5	Johann Eder, Claus Dabringer, Michaela Schicho, et al.: Data Management for Federated Biobanks. 2009 LNCS(DEXA).

Partner 27 – P3G – Lead contacts: Prof. Bartha Maria Knoppers and Dr Isabel Fortier

P3G (Public Population Project in Genomics) is a not-for-profit international consortium aiming to facilitate networking between population-based bio-clinical studies. Incorporated in 2004 under the leadership of Professor Bartha Maria Knoppers and Dr. Thomas Hudson, P3G provides to the scientific community an easy access to expertise, resources and innovative tools. The fulfillment of the P3G mission is based on four targets: 1) FOSTER COLLABORATION between studies, organizations and investigators working in the field of population-based biobanking; 2) OPTIMIZE the DESIGN, set up and research activities of bio-clinical studies, 3) PROMOTE HARMONIZATION of the information collected and 4) FACILITATE TRANSFER of KNOWLEDGE. P3G counts 29 Charter Members (e.g. UK Biobank, NCI), 15 Associate Members (e.g. NHGRI, Genoma Espana) and 238 Individual Members from more than 40 countries. Knowledge and information, developed by P3G and its partners are shared with the scientific community through the P3G Observatory website (www.p3gobservatory.org). Up to 138 large population-based studies (involving more than 11 million participants) are documented on the website, which also provides access to a series of tools aiming to support the development and harmonization of bio-clinical studies.

Since advising GenomEUtwin on the ethical issues associated with the creation of federated databases, Prof. B.M. Knoppers, leading the Centre of Genomics and Policy (CGP: formerly CRDP, Université de Montréal), has been an active partner in PHOEBE and now ENGAGE. While working in other areas as well (e.g. reprogenetics; pediatric research, etc.), it brings particular expertise in four fields related to BioSHaRE-EU: privacy; retrospective access to samples and data; genetic epidemiology and the ELSI issues associated with international harmonization in biobanking. In 2009, the CGP became the home to both the policy office and the data access compliance office of the ICGC (International Cancer Genome Consortium). Privacy compliance for all requests to the virtual ICGC database as well as the policy instruments for the Consortium itself are prepared at the CGP. For ENGAGE, data sharing agreements, publication and IP policies as well as the ELSI consent issues surrounding the need for retrospective access for meta analyses are ongoing activities. Genetic epidemiology and the ELSI tools for population endeavors were created through participation in PHOEBE, and, the generic prospective consent, data access and material transfer agreements for P3G. Population biobanking and associated issues are central to the CGP (see PopGen part of the HUMGEN International- a database dedicated to the compilation of international policy statements available at http://www.humgen.org). Under the direction of Dr Isabel Fortier (co-leader, WP1.2), the DataSHaPER team (Data Schema and Harmonization Platform for Epidemiological Research) will provide support and expertise for: (1) the documentation of current practices and available standards; (2) the assessment of the potential to share information between biobanks (including development of specific rules to assess potential to share) (3) the facilitation of the processing and pooling of information. The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Prof. Knoppers	McGill University	Ethics, international policy, population genetics
Dr. Isabel Fortier Prof. Avard	McGill University	Knowledge transfer, clinical and research ethics
Prof. Wallace	McGill University	Biotechnology, law, public health genomics
Prof. Joly	McGill University	Intellectual property, privacy, data management
Ma'n Abdul-Rahman	McGill University	ELSI, population genetics
A.-M.Tassé	McGill University	Bioethics, health law

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Knoppers, B.M. and C. Laberge, "Return of "Accurate" and "Actionable" Results: Yes!", Commentary on Target Article: "Public Expectations for Return of Results from Large-cohort Genetic Research", 9(6-7)

	(2009) The American Journal of Bioethics, 107-109.
2	Knoppers, B.M., "Genomics and policymaking: from static models to complex systems?", 125(4) (2009) Human Genetics, 375-379.
3	Wallace, Susan, Stephanie Lazor and B.M. Knoppers, "Consent and Population Genomics: The Creation of Generic Tools", 31(2) (2009) IRB: Ethics & Human Research, 15-20.
4	Horsman, D., B. Wilson, D. Avard, W. Meschino, C. Kimsung, M. Plante, A. Eisen, H. Howley, J. Simard, National Hereditary Task Force, "Clinical Management Recommendations for Surveillance and Risk Reduction Strategies for Hereditary Breast and Ovarian Cancer among Individuals Carrying a Deleterious BRCA1 or BRCA2 Mutation" Journal of the Society of Obstetricians and Gynecologists of Canada, 2007; 29(1): 45-60.
5	Gurwitz, David, Isabel Fortier, Jeantine E. Lunshof, B.M. Knoppers, "Children and Population Biobanks", 325(5942) (2009) Science, 818-819.

Partner 28 – Istituto Superiore di Sanità, (ISS) Rome – Lead contact: Dr. Giovanni Migliaccio

The ISS is the technical arm of the Italian Health Ministry with regulatory, inspective and coordination activities under its mandate. Both therapeutic and research biobanks are actively coordinated by the ISS in cooperation with the Regional authorities and the National Health Services institution. The activities of the Italian biobanks for research are aggregated in national networks in order to maximize the collection of the samples and to harmonize the criteria to define, collect, manipulate, store and release human biological samples for research. The European Collaborative Network of clinical and research Centres on Angiology/ Vascular Medicine is organized according to common diagnostic criteria and methodology. The samples from the EBPp Network are centralized. External collaboration is welcome under project's agreement and using VAS SOP and MTA. Samples and data within the isolates network are exchanged, with proper privacy safeguards, with other EU groups involved in studies on isolated populations (UK, The Netherlands, Sweden, Croatia, Estonia, etc.). The NIPAB samples that can be exchanged are those that are usually stored in hospital pathology archives (biopsy and surgical origin). Participation in tissue exchange is at the moment on a collaborative and voluntary basis. The tissues are also related with clinical record information. MHB is an operational model of hospital networked biobanking connected with a national hub. A core cryostorage facility can be used by all hospital specialties and departments, supporting biobanking at reduced costs. We have documented the availability to share biological samples based on a common MTA model from 20 research groups and performed validation studies on monitoring transportation temperatures during international shipments of cord blood. RIBBO is network of biobanks dedicated to the collection and storage of oncological samples funded and developed by the national Alliance Against Cancer (ACC). Cold storage of well characterized oncological samples collected under harmonized standard procedure which are available for sharing under collaborative research agreements.

The following principal scientific and/or technical personnel are involved:

Name	*Affiliation*	*Expertise*
Giovanni Migliaccio	Istituto Superiore di Sanità, ISS	Epidemiology, biobanking
Paolo Roazzi	Istituto Superiore di Sanità, ISS	IT management, database maintenance and design
Mariella Catalano	European Biobank on Peripheral Arterial Disease Patients - EBPp	Peripheral Arterial Disease, Vascular Diseases, Angiology/ Vascular Medicine
Paolo Gasparini	Italian Network of Genetic Isolates - INGI	Isolated populations
Giorgio Stanta	Network of Italian Pathology Biobanks - NIPAB	Archive tissues; new fixatives; molecular analysis in FFPE
Paolo Rebulla	Multispecialty Hospital Biobank	disease biobank; stem cells; informed consent
Angelo Paradiso	Italian Network of the Oncologic BioBanks	Oncologic samples

Relevant publications:

	Authors, Title, Name journal, Year/issue/pages
1	Nelis M, et al. Genetic structure of Europeans: a view from the North-East. PLoS One. 2009;4(5):e5472. Epub 2009 May 8.
2	Sala C, et al. Variation of Hb levels in normal Italian populations from genetic isolates. Haematologica, 2008 Sep;93(9):1372-5
3	G Stanta, S Pozzi Mucelli, F Petrera, S Bonin, G Bussolati, "A novel fixative improves opportunity of nucleic acids and proteomic analysis in human tissues", Diagn. Molec. Pathol 15:115-23;2006
4	G Stanta, A Cescato, S Bonin, R Barbazza, "Bioethics considerations for medical research in human archive tissues: the point of view of the researcher." Virchows Arch.;453:117-9; 2008

5 Salvaterra E et al. Banking together. A unified model of informed consent for biobanking. EMBO Rep. 2008;9:307-13.

2.3 Consortium as a whole

The work during BBMRI-PP built on previous and ongoing national, European and global projects and initiatives, such as research projects funded under FP5 and FP6 as well as new projects under FP7, public/private partnerships (PPPs) which are directly related to the needs of BBMRI, work on biobank harmonization done by the P³G and PHOEBE consortia, the strategic research agenda of the Innovative Medicines Initiatives, the WHO, and the OECD initiative on a global network of Biological Resource Centres. The basic BBMRI-PP principle has been one of subsidiarity: integrating and harmonizing biomolecular resources and molecular tools with complementary national and regional biobank formats, each with its own strengths, to render their combination much more powerful than each resource type alone.

In the next period, the BBMRI community aims to ensure that the quality and clinical annotation of biological samples, as well as their accessibility to the user community, meets the requirements of current and future analysis tools. This will provide the best research opportunities to define and correlate healthy, pre-clinical and clinical profiles, and will strongly boost the integrated study of biological and genetic disease mechanisms, improve the delineation of clinical phenotypes and establish biomarker spectra for disease prognosis and therapy monitoring. If properly funded in the impending construction phase, BBMRI can be stabilized and extended into a major resource of wide strategic and practical utility, both in the biomedical arena and – through pioneering work in biospecimen storage and provision – also in the wider field of the life sciences. This will give European scientists, industry and citizens distinct advantages, such as

- broad and unified access to the catalogued information on biological samples and collected data, which before the emergence of BBMRI was cumbersome and due to different, fragmented data structures and incompatible regulations for their access and exchange in different countries,
- a setting to establish an open-source (code) based federated database structure that can guarantee the same standard of data quality in annotation while protecting donors' privacy,
- a structure to provide access to a Europe-wide data and sample set for investigators thus providing data with better statistical power or permitting the investigation of rare or highly diverse diseases,
- capacity and code of conducts to develop prospective collections meeting the needs of particular research projects or clinical trails, based on Europe-wide networking of biobanks meeting compatible quality standards,
- compliance with, as well as further constructive alignment of, ethical and legal requirements,
- sound governance system building on input by all stakeholders,
- ultimately, a solid funding scheme for up keeping and updating of the resources.

In order to make a smooth transition from the preparatory phase to the construction phase of a pan-European Biobanking Infrastructure, it should be realized that the biobank landscape in Europe, as it was – and still is - inventorized by BBMRI, is extremely diverse. On one hand there are large, regionally and nationally well-established facilities, often population-oriented, with a long history and a high publication track record, and also smaller, but equally well-established and -organized clinical biobanks with great, disease-specific information depth. On the other hand there is a great variety of smaller biobanks, maintained in hospitals by clinical experts with a specific focus or research question, often on a voluntary basis and with a more fragmented funding history. A recent development - in part caused by the member states' attention for the ESFRI process and the impact of BBMRI in this context – has been the targeting of major national funds towards the establishment of newly conceived, large and well-equipped biobank. There can be transversal and population-based, like Biobank-UK, or clinically-oriented and prospective, like the Dutch Pearl String Initiative.

Considering these field dynamics, it was deemed appropriate to focus the next step in the BBMRI establishment on the enlisting of the key, large-scale European biobanks, i.e. the mature parties who have also played a trailblazing role in the BBMRI-PP, in the delivery of a proof-of-principle to provide widespread access of interested users to their data and samples. This optimally fits the present call under the FP7-INFRASTRUCTURES heading, which has as one of its aims to 'provide support to existing research infrastructures' in the form of a 'combination of collaborative projects and coordination and support actions for integrating activities'. Specifically, this proposal in is response to the topic: **INFRA-2010-1.1.12: 'Large-scale biobanks for clinical and epidemiological studies'.**

The main goals specified under this heading are

- to provide access to samples and data for clinical and epidemiological studies.
- to enhance cataloguing (e.g. of samples, tools and methods),
- to develop tools for enhancing access to data and samples,
- to address the harmonisation of Ethical, Legal and Social Issues (ELSI).
- that such a project will be structured in coordination with the ESFRI "BBMRI" project.

The aim of this present proposal is to fulfil exactly the above mentioned goals. It is optimally served by focusing on the more advanced biobanks and the BBMRI core community, who are well-integrated in the BBMRI infrastructure as established in the Preparatory Phase. They can serve as a prototype which can later be extended, with additional funding of mainly national but also pan-European nature, to expand the access logistics once it has achieved a robust format, informatically, technologically and ethically, as explored and implemented through the present I3 call.

Other countries:
P3G is based in Canada and has a long standing cooperation with several core partners in BBMRI. They are several years the leading authority in worldwide biobanking and have unique expertise.

2.4 Resources to be committed

Requested resources

The resources to be directly committed to this proposal are summarized as follows:

WP1.1	Category	Costs		WP1.8	Category	Costs
	Personnel	855,600			Personnel	110,400
	Governance board	70,000			Meetings	6,000
	Scientific and ethical advisory	27,000			Teleconferences	500
	Stakeholder-user conference	60,000			**direct costs**	116,900
	Travel	50,000			+ 7 % indirect costs	8,183
	Other (web. PR mat. &act, etc)	115,000			**Requ. EC**	**125,083**
	direct costs	1,177,600				
	+ 60% indirect costs	706,560				
	Subcontracting	200,000				
	Requ. EC	**2,084,160**				
WP1.2	**Category**	**Costs**		**WP1.9**	**Category**	**Costs**
	Personnel	165,600			Personnel	110,400
	Meetings	6,000			Meetings	6,000
	Teleconferences	500			Teleconferences	500
	direct costs	172,100			**direct costs**	116,900
	+ 7 % indirect costs	12,047			+ 7 % indirect costs	8,183
	Requ. EC	**184,147**			**Requ. EC**	**125,083**
WP1.3	**Category**	**Costs**		**WP2.1**	**Category**	**Costs**
	Personnel	202,400			Personnel	1,545,600
	Meetings	6,000			Meetings	33,333
	Teleconferences	500			Teleconferences	1,333
	direct costs	208,900			Software Licensing	66,667
	+ 7 % indirect costs	14,623			**direct costs**	1,646,933

	Requ. EC	**223,523**			+ 60% indirect costs	988,160
					Requ. EC	**1,976,320**
WP1.4	**Category**	**Costs**		**WP2.2**	**Category**	**Costs**
	Personnel	469,200			Personnel	165,600
	Meetings	14,000			Meetings	10,667
	Teleconferences	1,000			Teleconferences	667
	European training courses	140,000			**direct costs**	176,933
	Curriculum development	40,000			+ 60% indirect costs	106,160
	direct costs	664,200			**Requ. EC**	**212,320**
	+ 7 % indirect costs	46,494				
	Requ. EC	**710,694**				
WP1.5	**Category**	**Costs**		**WP2.3**	**Category**	**Costs**
	Personnel	257,600			Personnel	276,000
	Meetings	6,000			Meetings	8,000
	Teleconferences	500			Teleconferences	667
	direct costs	264,100			**direct costs**	284,667
	+ 7 % indirect costs	18,487			+ 20/ 60% indirect costs	146,000
	Requ. EC	**282,587**			**Requ. EC**	**323,000**
WP1.6	**Category**	**Costs**		**WP3.1**	**Category**	**Costs**
	Personnel	202,400			Personnel	460,000
	Meetings	12,000			Meetings	14,000
	Teleconferences	2,000			Teleconferences	1,000
	direct costs	216,400			Access cost	1,000,000
	+ 7 % indirect costs	15,148			**direct costs**	1,475,000
	Requ. EC	**231,548**			+ 7 % indirect costs	33,250
					Requ. EC	**1,508,250**
WP1.7	**Category**	**Costs**		**WP3.2**	**Category**	**Costs**
	Personnel	78,200			Personnel	607,200
	Meetings	6,000			Meetings	14,000
	Teleconferences	500			Teleconferences	1,000
	National experts	204,000			Access cost	1,000,000
	direct costs	288,700			**direct costs**	1,622,200
	+ 7 % indirect costs	20,209			+ 7 % indirect costs	43,554
	Requ. EC	**308,909**			**Requ. EC**	**1,665,754**

Access cost

For transnational access, 11 prototype biobanks, both population based and clinical, have been identified as being of the most mature and comprehensive biobanks in Europe. Through years of strong efforts, biological samples have been collected and stored for a wide-spread number of diseases in clinical biobanks and a very large number of participants have been screened and included in the population based biobanks. These biobanks are often established on the bases of health surveys with a broad scope towards common health and common, but often complex diseases.

Sample handling is particularly challenging in order to preserve sample quality and prevent deterioration. It has required, and will also in the future, require extensive resources to run and maintain these biobanks at a state-of-

the-art-level. These expenses, both in terms of specialized personnel and advanced technological solutions have mainly been covered by the institutions themselves which will also be the case onward. Amongst the participating partners, funding is also gradually more available on a national level to strengthen the national hubs and infrastructure, such as the BBMRI.NL, BBMRI.SE, BBMR.NO, BBMRI.xx.. Building of national biobank infrastructures will constitute a strong and necessary basis for DIAL-BBMRI, which has also been so for the success of BBMRI-PP.
In complement with the EC contribution, these resources – which are committed or in the decision process, with similar decisions to come in other EU countries - are a major extra asset to warrant the future success of DIASL-EU-BBMRI to achieve is goals In compliance with the transnational access fees and budgeted unit costs, this will enable this infrastructure to offer high-quality samples at very low costs to applicants.
In conjunction with the biological sample, health related information, individual exposure data and eventually validated disease development will be available for the EU. This is made possible through variety of time consuming and costly procedures, also including linkage to health records and regional and national registries. For the prototype biobanks in DIAL-BBMRI, these resources will also be available along with the biological samples, increasing the scientific value extensively, but without increasing the costs. Typical costs of running health-surveys and screening studies may be illustrated by the costs of close to € 80 million for the ongoing UK biobank study - available for DIAL-BBMRI in 2011/2012 - € 60 million for the Dutch Lifelines study – partly available in 2010 and fully in 2012 - and € 20 million for the recently completed HUNT 3 study. The actual running costs of the corresponding biobanks are not included.

The only way of securing an adequate financial plan of DIAL-BBMRI, will be the low cost contributions from all the institutions entering their mature biobanks into the project. Below, both the staff effort and other major costs are illustrated as a typical contribution from the prototype biobanks

Population Biobank Prototype	Subjects x1000	Samples x1000	Lab engineers FTE	Total staff FTE	Annual running budget x1000	Annual technological Investments X1000
Norway HUNT/CONOR	300	4 500	10	25	€ 3000	€ 1000
Germany KORA	18	320	3	10	€ 500	€ 200
Netherlands, BBMRI-NL	500	6 000	~ 20	>40	€ 12 000	~€ 10 000
Finland, THL DNA Biobank	200	600	5	8	€500	€500
Sweden BBMRI.SE	110	500				
UK UK Biobank	500	15 000	Available from 2011			
Estonia EGPUT	40	922	5	22	€ 1300	€ 1700
Spain BN ADN	7.5	25	15	20	€ 1000	€ 200

,

Clinical biobank Prototype	Subjects x1000	Samples x1000	Lab engineers FTE	Total staff FTE	Annual running budget X1000	Annual technological Investments X 1000
Germany	38	190	6	18	€ 1 200	€ 600
Netherlands	157	470	15	45	€ 3 000	€ 3 000
Austria	1 000	3 700	15	25	€ 3 000	€ 3 000

UK	22	37	3	6	€ 500	€ 200
Spain	46	121	40	70	€ 11 000	€ 400
Italy	48	440	41	114	€ 4 300	€ 1 200
France	153	1 360	20	30	€ 4 000	€ 2 000

3. Impact

3.1 Expected impacts listed in the work programme

DIAL-EU-BBMRI directly contributes to the integration of the key large-scale bio-banks in Europe and will provide access to samples and data for clinical and epidemiological studies.
DIAL-EU-BBMRI builds further on the foundations that were made in BBMRI-PPI. The investments made by the European Commission and the Member States into the biobank and biomolecular infrastructure will be made more sustainable by DAIL-EU-BBMRI. To achieve durable integration and expected impacts DAIL-EU-BBMRI consists of three types of activities:

1. Networking activities to foster a culture of co-operation between research infrastructures and scientific communities and help developing a more efficient and attractive European Research Area. The networking activities describes in WP 1.2 to WP 1.9 aim:
   - to foster harmonisation and standardization,
   - to develop an open access web portal with databases of reagents and methods,
   - to develop a European Master/PhD curriculum in Management of Biological Resources,
   - to foster strategic coordination between this project and BBMRI/BBMRI-PPI, other relevant initiatives on the ESFRI roadmap and for instance the Innovative Medicines Initiative
   - to foster the global biobank coordination by identifying key initiatives to interface with, to develop a strategic integration plan for systematic and regular inter-project communication and to develop a strategic horizon scanning plan for the science and the societal issues
   - to develop and update contents of the Wiki Legal Platform
   - to foster quality assurance
   - to organise stakeholder/user meetings and to take steps forward to develop a one-stop-portal for access.

2. *Joint research activities*, to improve, in quality and/or quantity, the services provided by the infrastructures. These joint research activities described in WP 2.1 to 2.3 aim:
   - to develop a federated database system that enables searching for interesting and comparable material across European Biobanks
   - to research biobank technologies and infrastructure technologies in order to achieve the design and development of a comprehensive Laboratory Information Management Systems (LIMS)
   - to develop legal and ethical positions ???
3. *Trans-national access and/or service activities, to support academic and industries in their access to the research infrastructures in the consortium. The access activities described in WP 3.1 and 3.2 aim to give access to:*
   - Population biobank data and samples, and
   - Clinical biobank data and samples

All these activities directly enhance the cataloguing (e.g. of samples, tools and methods), will develop tools for enhancing access of data and samples and will address the harmonisation of ethical, legal and social issues (ELSI).
DAIL-BBMRI consists of the more advanced biobanks and the BBMRI core community, who are well-integrated in the BBMRI infrastructure as established in the Preparatory Phase. They can serve as a prototype which can later be extended, with additional funding of mainly national but also pan-European nature, to expand the access logistics once it has achieved a robust format, informatically, technologically and ethically, as explored and implemented through the present I3 call.

Further scientific and socioeconomic impacts
Biobanks are increasingly seen as an essential tool in translating biomedical research. Biobanks provide researchers with the biological samples and therefore make large-scale research possible. Based on the information from biobanks, researchers can explore why some people develop particular complex diseases while

others do not. Biobanks allow researchers to investigate how each person's lifestyle, environment, and genes impact the progression of particular diseases. Possessing the knowledge of how the disease is triggered enables researchers to make more precise diagnosis and design better targeting treatment strategies.

BBMRI will contribute to the scientific excellence of Europe as a whole by providing Investigators' access to high quality biological resources and data for:

- Participants in current and future EU framework programme Health projects.
- Epidemiologists, clinicians, geneticists, pathologists and molecular biologists in national centres of excellence.
- Pharmaceutical and biotech industry

The implementation and development of its "distributed hub structure" which is designed to allow the extension of the infrastructure by incorporating existing and new components that meet the criteria of excellence of BBMRI and DAIL-EU-BBMRI and that have physical locations in the convergence regions as well as the outermost regions thus providing a pan-European solution.

In short, DIAL-EU-BBMRI ensures that biobanks are developed and used to their full potential for European citizens and their health, European academics and European industries while keeping in mind ethical, social and legal aspects

3.2 Dissemination and/or exploitation of project results, and management of intellectual property

The results and standards generated by DIAL-BBMRI will be disseminated in public meetings, most importantly the general stakeholder meetings, but also meetings specifically tailored to the individual stakeholder communities, through various reports and a dedicated website. The dissemination of DIAL-BBMRI will be based on the dissemination plan of BBMRI/BBMRI-PPI and improved there where necessary. One of the central aims of DIAL-BBMRI is the dissemination of its work to reach the Scientific Community, the BBMRI community, those parties responsible for policymaking and implementation of the developed guidelines, but most importantly the general public and broader stakeholder groups. Dissemination of the DIAL-BBMRI project is a core activity and therefore is linked to all the work packages in the project.

The DIAL-BBMRI target groups are:

The BBMRI community consisting of 51 Scientific Partners, 24 Funding Organisations (Ministries, and research councils) and more that 200 Associated Partners (such as hospitals and Academic Medical Centres that would like to connect their biobanks to the BBMRI infrastructure). This community is a very comprehensive group of experts and end users in the field of biobanking in Europe.

The Scientific community (including industry) is a broader scientific stakeholder group with general interest in the biobanking field who will greatly benefit from the guidelines and information that is shared during the course of the DIAL-BBMRI project and who will be extensively included in our dissemination plan. This group consists of fundamental scientists, clinical scientist and industry involved in pharmaceutical and biomedical research, who will be informed appropriately, though where necessary will also be asked to give expert feedback to the project.

The Policy makers involved in the fields of biomedical research, ethics and the legal and societal landscape in Europe will be widely informed and asked for guidance regarding future harmonization of regulations during the course of the project and included in a variety of communication activities.

The General public (including patient groups) consists of all parties interested not mentioned above, but these stakeholders are of the outmost importance, because the data and samples of this group is the central component of the DIAL-BBMRI project. This stakeholders group is also key to the discussion regarding ethical considerations regarding data and sample collection, but also requires a transparent communication and accountability regarding the funding as this project is funded by public resources.

Communication tools:

The DIAL-BBMRI will make use of a comprehensive communication package with a variety of tools in order to disseminate the project to all stakeholder parties appropriately. The various communication tools used are linked to the appropriate stakeholder groups as explained below.

Conferences

Annual DIAL-BBMRI general meetings will be organised where outstanding challenges in harmonization, standardization and calibration will be discussed, progress in research and development as well as access provision. Also the various communications tools, such as provided by P3G and other initiatives and the "repository of methods" will be presented, to create interest and disseminate the outcomes of DIAL-BBMRI to stakeholders. Finally, and of key value in the translational process, a joint stakeholders and users conference will be held twice, once relatively early around mo 14 to establish the dialogue on what has been achieved thus far, and once later in the project, but timely enough to utilize the views on the advancements in the final phase.

Website

The website for DIAL-BBMRI will be developed according to the already existing BBMRI-EU website with identified improvements and will also be linked directly to ensure continuity between BBMRI and DIAL-BBMRI.
The DIAL-BBMRI website has a direct link to the already existing P3G observatory, an online web based tool that serves as repository of methods and tools for harmonization, standardization and calibration in the field of biobanking, which will be further developed and expanded during the course of the DIAL-BBMRI project.

Stakeholders forum

The website also contains a stakeholders forum in order to get continual feedback on the dissemination plan from all the stakeholders that will make it possible to improve on the dissemination plan during the course of the DIAL-BBMRI project

WIKI legal platform

The website will also contain a platform to communicate and inform all the stakeholder parties regarding legal and ethical issues related to the DIAL-BBMRI project.

Meetings and training workshops for specific stakeholders and users:

Various meetings and training workshops will be organised during the course of the DIAL-BBMRI project, these include patient organisation training workshops, international biobanking training courses for end users, workshop with non-European biological resource centres and workshops with IMI-EFPIA representatives and IMI-coordinators.

Reports and publications

DIAL-BBMRI aims for a transparent and open communication. In order to achieve this objective DIAL-BBMRI will report and publicise its results timely regarding ethical, legal and societal issues as well as all its RTD activities in appropriate reports or other publication forums. This includes for example open access guidelines, ethical guidelines and biomedical research results.

Management of IP

IPR Management is an integral subject of BBMRI, DIAL-BBMRI and broader BBMRI community. IPR identified in RTD activities is dealt with as per usual and owned by the person or organisation that has identified the IPR. This will be comprehensively addressed in the consortium agreement of DIAL-BBMRI.
IPR management regarding open access will be comprehensively addressed in the open access agreement. The open access IPR management is one of the key subjects that requires EU guidelines, harmonisation and standardisation, which will be further developed in the course of DIAL-BBMRI. The parties who wish to deposit

or use the open access to samples and data will have to be included and abide by the open access agreement and EC funding will only be available to those parties who have done so.

4. Ethical Issues

Ethical issues linked to the use of human samples, use and exchange of human samples and data, including genetic data in an international context and issues associated with the public release of certain results are the core ethical issues at stake in this project. They have previously been thoroughly explored in the context of a number of several other projects where most of the applicants of DIAL-BBMRI participated. The DIAL-BBMRI proposal builds on the work done within the BBMRI preparatory phase (PP) and will deliver key tools for the implementation of BBMRI under the ERIC legal entity (BBMRI-ERIC) and serves as a proof-of-concept for accessing BBMRI resources and services. Hence the ELSI work performed in BBMRI-PP will be the basis of the DIAL-BBMRI ELSI work. Besides classical tissue exchanges and usages, genotyping and sequencing projects are going to develop as well as projects involving molecular tools and high-throughput analysis platforms for sample analysis to investigate genes, proteins and metabolites in biobanked samples.
Most of the work in DIAL-BBMRI will be developing procedures, standards and harmonised platforms and coordinating with other initiatives without many actual exchanges and experimental manipulations in the first part of the project (networking). Only biological samples for quality control and setting the protocols will actually be transferred between countries and used in coordination WPs (WP1). The second part of the project dealing with joint research will not involve exchange of samples but will pilot procedures especially IT procedures that will meet the requirements of an optimal use of bioresources; but the first requirement indicated (see WP2.1) is ensuring the confidentiality of donors data. The various kinds of data produced will be the subject of various levels of protection. The third part of the project (Integration) is a prototype where procedures will have to be validated and will involve actual samples and data exchanges and operation. DIAL-BBMRI requires developing and addressing integration of complex complementary data with both new technological aspects by DNA and RNA sequencing, proteomic data and various phenotypic data.
So ethical dimensions will be taken into account at 3 levels1) as part of the parameters to take into account with high priority in all tools for coordination/education/standardisation/quality produced; 2) as research object where debates and uncertainty or new ethical challenges appear and policy is not stabilised; 3) as requirement for implementation of tools and procedures in the prototype DIAL-BBMRI.

The ethical aspects are dealt with very seriously in the project and are indeed embedded more precisely as follows:

1. management and governance structure
    - A scientific and ethical advisory board will include ethical expertise independent from the project
    - The sample and data access committee will have requirements regarding ethics as mandatory elements (applicants will have to provide copies of approval from the relevant research ethics committee, informed consent and data authority permission). A procedure for checking the compatibility between the informed consent and the use proposed will be set up.
    - Each periodic report will contain a substantial ethics report, that will allow to follow up with the realisation of the project from this point of view
2. in the project itself
    a. operational level A full WP (WP1.7) is devoted to setting up a Wiki platform for legal information relevant for the project. The mission of the WIKI Legal Platform is to properly embed the pan-European Biobanking and Biomolecular Resources Research Infrastructure (DIAL-BBMRI) into the European legal framework, by providing the community with immediate access to validated legal templates. Thanks to a vast cooperation and network of legal experts in this domain an updated legal information on consent, data protection, access policies, feedback, tissue transfers, data transfers, IP and benefit sharing will be provided; validated templates such as consent forms, MTA, etc. adapted to the various countries and supra national level will be provided, according tot he kinds of biobanks considered; besides updated and validated legal information will be provided. This platform will build on its first version developed for BBMRI-PP in its ELSI WP6 (www.legalpathways.eu) and on the available tools in the domain, such as for example hSERN – human sample exchange regulation navigator

(www.hsern.eu) , a tool to provide validated and systematically organised information on legal requirements for exchanging biological samples for research across borders in Europe. As a matter of fact the heterogeneity of the legal requirements in the various countries could hamper the exchanges or create legal uncertainty. Persons well aware of these aspects are actively involved in the consortium (Jasper Bovenberg, NL; Jane Kaye, UK; Bartha Knoppers, Canada; Emmanuelle Rial-Sebagg, France).

b. coordination level All WP underline how they will incorporate ethical aspects in their work; this is true especially for the training and dissemination WP 1.4, but also the technical WP where quality aspects or bioinformatics protocols include an ethics component that will be worked out together with the relevant persons in the consortium. In the educational material, case studies examples illustrating the ethical issues encountered in different biobanks will be worked out as educational material. Internationally recognised figures in the domain of ethical aspects of biobanks are among the participants from Canada (BM Knoppers), France (A Cambon-Thomsen), UK (J Kaye) and others; they all have a strong network of collaborators.

c. research level. An entire research WP (WP2.3) on legal, ethical and societal positions is proposed and will allow to explore deeply the aspects where agreement at international, at least European level is not reached (for example the use of children samples and data in long term biobank based research)

- the domains that were not addressed in BBMRI-PP and that may need to be considered in the future. The fact of addressing the ethical aspects of issues like cord blood banking, cell lines and stem cells banking for research before these cases actually exist in BBMRI shows the prospective view the consortium is paying to ethical aspects. In the same spirit this WP2.3 will address the various dimensions attached to the results and findings that will come out of the increasing international use of samples and data.

- regular discussion meetings on the issues at stake are planned in order to raise awareness of the consortium.

- an important feature is the dimension on empirical research on the attitudes and opinions of European citizens regarding biobanking; positions on ethical aspects will be explored. This consultation process will give a real embedment of policy options proposed in reality and opinions of those concerned, whereas many preceding projects were disregarding this dimension that is still poorly documented

- Finally this WP will propose governance models adapted to the various cases of biobanks and their uses, taking into account the ethical dimensions.

b) at the implementation level

- The prototype in WP3 will concern both clinical based and population based biobanks. This will be the validation part to test the accuracy and viability of all standards, harmonising tools and procedures produced.

- The corresponding WP3.1 and WP3.2 have set as mandatory and priority tasks the procedures to verify the compliance with the legal and ethical requirements and collaboration with WP1.7 and 2.3 will be lively. The countries involved and the responsible persons are

1. **Prototype Austria (Kurt Zatloukal)**
2. **Prototype Estonia (Andres Metspalu)**
3. **Prototype Finland (Leena Peltonen/ or Markus Perola)**
4. **Prototype France (Georges Dagher)**
5. **Prototype Germany (Erich Wichmann)**
6. **Prototype Italy (Giovanni Migliaccio)**
7. **Prototype Netherlands (Gert-Jan van Ommen)**
8. **Prototype Norway (Kristian Hveem)**
9. **Prototype Spain (Alberto Orfao)**
10. **Prototype Sweden (Joakim Dillner)**
11. **Prototype UK (Bill Ollier).**

All these countries have legal provisions that apply to biobanks for research either through specific acts (Estonia, Norway, Sweden, UK) or in the corpus of legal provisions for biomedical research and/or bioethics and/or consider the opinion of their National Ethics Committee on the subject (Austria, Finland, France, Germany, Spain, Italy, Netherlands). Each national node has set an information desk on national requirements.

In addition to the Wiki legal platform (WP1.7) a resource as societal platform giving also access to expertise and up to date information in ethical challenges and in society perception, and proposing specific activities and resources will be set up as part of the ERIC, inspired by the models of the Toulouse societal platform (http://societal.genotoul.fr/) and the Humgen Canadian website and P3G, observatory for the service of the community of DIAL-BBMRI and in order to facilitate awareness and to stimulate the debates.

In addition to adhering strictly to national provisions, and putting in place the necessary measures to ensure this is the case in the protocols, the members of the consortium will rely on the international available relevant texts they are well aware of to set up the infrastructure policy and operation mode.

Participants and protocols set up in DIAL-BBMRI will conform to relevant EU legislation including:

- The Charter of Fundamental Rights of the EU, December 2009;
- Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data;
- Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions.

Each node, under the responsibility of the person in charge (see above list) will be held responsible for fulfillment of all legal and ethical requirements in his/her country. If warranted by national legislation, protocols that are used in the network need to be submitted to and approved by local research ethical review committees. All procedures will be set up with approval from the SEAB and all applicant projects or biobanks need to deliver the relevant approval to the sample and data access committee that will ensure compliance with the procedures set up.

International conventions and declarations

Participants will respect the following international conventions and declarations, as appropriate:

- Helsinki Declaration in its latest version (2008);
- Convention of the Council of Europe on Human Rights and Biomedicine signed in Oviedo on 4
- April 1997, and the Additional Protocol on biomedical research (2005) signed in Strasbourg 25/1/2005
- UN Convention on the Rights of the Child, as from 1989;
- Universal Declaration on the human genome and human rights adopted by UNESCO (1997);
- Universal declaration on human genetic data adopted by UNESCO (2003)
- Participants should take into account to the opinions of the European Group of Advisers on the
- Ethical Implications of Biotechnology (1991 -1997) and the opinions of the European Group on
- Ethics in Science and New technologies (as from 1998), especially Opinion 11 (1998) on Ethical aspects of human tissue banking;

Where relevant for setting the policies in WP2.3, the following opinions will also be considered for any stem cell regulation: opinion 15 (2000) on Ethical aspects of human stem cell research and use; opinion 19 (2004) on Ethical aspects of umbilical cord blood banking ; and opinion 22 (2007) on The ethics review of hESC FP7 research projects; as for regulations relevant for WP1.3 dealing with catalogue of reagents, where relevant the participants will take into account any relevant recommendations made in the 2 following opinions on distinct but potentially overlapping fields regarding biomolecular reagents: Opinion 21 (2007) on Ethical aspects of nanomedicine and the recent opinion 25 (2009) on The ethics of synthetic biology.

- The Council of Europe additional Protocol to the European Convention on Human Rights and
- Biomedicine on Biomedical Research (CETS No.:195, 2005);
- In addition the Council of Europe recommendation regarding the use of human biological samples
- in research (Rec (4) 2006) will be followed.

- Recommendation R (79) 5 of the Committee of Ministers to member States concerning international exchange and transportation of human substances
- Recommendation R (94) 1 of the Committee of Ministers to member States on human tissue banks
- Recommendation (97) 5 of the Committee of Ministers to Member States on the protection of medical data

Finally the recently appeared OECD guidelines on human biobanks and genetic research databases (Oct 2009) will be followed as they address many aspects ethically relevant.

Description of the potential ethical aspects of the proposed research regarding its objectives, the methodology, and the possible implications of the results

As indicated in the ethical issues table, ethical and legal issues in DIAL-BBMRI might arise from the use of already collected human tissues and data as well as from newly constituted collections. These tissues and data will always come from ethically approved projects. The consortium does not perform research on human embryos, fetuses, children or animals. The issues of children sample and data usage and those linked to cord blood or other stem cells an cell lines will not occur during DIAL-BBMRI at the prototype level, but they are prospectively addressed in WP2.3 in order to have discussed policy options and protocols in case this happen in the future. So the consortium prospectively consider possible future ethical issues. No developing countries are involved and no dual use is foreseen. Privacy issues are addressed in several work packages and especially the work package WP2.1 on bioinformatics that carefully plan specific tasks to ensure confidentiality issues. The tests of these procedures in the prototype will be carefully monitored in order to gain experience from this and to amend the procedures if needed.

In conclusion ethical aspects are integral part of the project at all levels.

ETHICAL ISSUES TABLE

(Note: Research involving activities marked with an asterisk * in the left column in the table below will be referred automatically to Ethical Review)

	Research on Human Embryo/ Foetus	YES	Page
*	Does the proposed research involve human Embryos?		
*	Does the proposed research involve human Foetal Tissues/ Cells?		
*	Does the proposed research involve human Embryonic Stem Cells (hESCs)?		
*	Does the proposed research on human Embryonic Stem Cells involve cells in culture?		
*	Does the proposed research on Human Embryonic Stem Cells involve the derivation of cells from Embryos?		
	I CONFIRM THAT NONE OF THE ABOVE ISSUES APPLY TO MY PROPOSAL	X	

	Research on Humans	YES	Page
*	Does the proposed research involve children?		
*	Does the proposed research involve patients?	X	
*	Does the proposed research involve persons not able to give consent?		
*	Does the proposed research involve adult healthy volunteers?	X	
	Does the proposed research involve Human genetic material?	X	
	Does the proposed research involve Human biological samples?	X	
	Does the proposed research involve Human data collection?	X	
	I CONFIRM THAT NONE OF THE ABOVE ISSUES APPLY TO MY PROPOSAL		

	Privacy	YES	Page
	Does the proposed research involve processing of genetic information or personal data (e.g. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)?	X	
	Does the proposed research involve tracking the location or observation of people?		
	I CONFIRM THAT NONE OF THE ABOVE ISSUES APPLY TO MY PROPOSAL		

	Research on Animals	YES	Page
	Does the proposed research involve research on animals?		
	Are those animals transgenic small laboratory animals?		
	Are those animals transgenic farm animals?		
*	Are those animals non-human primates?		
	Are those animals cloned farm animals?		
	I CONFIRM THAT NONE OF THE ABOVE ISSUES APPLY TO MY PROPOSAL	X	

	Research Involving Developing Countries	YES	Page
	Does the proposed research involve the use of local resources (genetic, animal, plant, etc)?		
	Is the proposed research of benefit to local communities (e.g. capacity building, access to healthcare, education, etc)?		
	I CONFIRM THAT NONE OF THE ABOVE ISSUES APPLY TO MY PROPOSAL	X	

	Dual Use	YES	Page
	Research having direct military use		
	Research having the potential for terrorist abuse		
	I CONFIRM THAT NONE OF THE ABOVE ISSUES APPLY TO MY PROPOSAL	X	

5. Consideration of gender aspects

Gender differences in the various diseases studied as well as gender composition of collections and cohorts studied will be examined as a systematic parameter. Gender aspects will also be discussed in the stakeholder forums. As a specific task on gender issues is part of BBMRI-PP WP6; results and findings on that level will be taken into account to set up the most efficient gender issues policy in DIAL-BBMRI.

The gender issues regarding the participation of both sexes in research, education and dissemination programs of the DIAL-BBMRI project will be carefully monitored all throughout the project.

Participants will involve young women researchers in their activities as well as young male researchers: the DIAL-BBMRI participants are committed to promoting equal employment opportunities and to actively participate in actions planned to make this policy fully effective. It is noteworthy that the scientific management of the DIAL-BBMRI project directly involves women as scientific team leaders; this is the case for J Harris (Oslo), BM Knoppers (Montreal), I Fortier (P3G, Montreal), A Cambon-Thomsen (Inserm, Toulouse, France), Leena Peltonen, (Cambridge, UK, and Helsinki, FI), Jane Kaye (HeLEX, UK). The project guarantees an as fairly -balanced representation of both sexes as possible amongst today's field leaders. Indeed, from the overall number of 32 lead contacts involved in the DIAL-BBMRI project, 25% are women. Globally, over 80% of the young scientists are young women. Besides, special care has been taken to improve the number of women in responsibility as two work packages are headed by women.

However, this fair distribution will not prevent us from educating the members on the impact of gender.

The DIAL-BBMRI project will strive to employ an equal number of women and men among the research staff, and make specific efforts to consider gender issues in recruitment practices. The target rate of 50%

of women employed at different positions (including top decision-making positions) will be monitored during the project. The objective is to maintain the participation rate throughout the project by implementing the specific gender action plan described below.

The project steering board and in particular the Executive Management Team will follow up the evolution of gender equality within the consortium and will contribute to raise awareness about gender issues in the workplace. WP1.1 will specifically dedicated to this aim. In particular the management team will ensure that participants are sensitized about gender issues and have access to relevant knowledge:

• The Executive management will conduct a survey at the beginning on the project - by the mean of a questionnaire distributed to all participants - in order to assess more precisely the gender balance within the consortium. The results of this survey will then be published on the project dedicated website.

• All relevant knowledge and documents (i.e. reports produced by the Helsinki group, results of the gender monitoring studies conducted in FP6, etc., but also links to public websites and European associations promoting gender equality), will be distributed to participants and made available on the intranet. The management team will provide support and additional information on gender aspects in research activities to participants needing it. The management team will also inform participants about relevant events (workshops, training sessions) organized on gender mainstreaming, and will encourage them to attend.

• DIAL-BBMRI participants will be sensitized to gender equality during meetings (kick-off meeting and General assemblies). Senior female researchers will be invited to give a presentation on their own experience, and members from European associations (such as European PWN (professional women's network, for example) will also be contacted and invited to attend. Participants will be encouraged to locally sensitize their staff regarding gender issues in the workplace and ensure that there is no gender discrimination within their teams, by undertaking concrete actions such as:

- Establishing a policy of equal gender opportunities.
- Favoring part-time positions and flexible working hours and patterns for men and women having families.
- Encouraging the reintegration of women that have taken time-off to raise their children,
- Providing support to young women researchers, by encouraging for instance mentoring relationships with male or female senior researchers from the DIAL-BBMRI consortium.
- Finally the management team will ensure that both women and men are well represented in the Scientific and ethical advisory board and other bodies of the project.