Deliverable D1.4

Project Title:	Building data bridges between biological and medical infrastructures in Europe	
Project Acronym:	BioMedBridges	
Grant agreement no.:	284209	
	Research Infrastructures, FP7 Capacities Specific Programme; [INFRA-2011-2.3.2.] “Implementation of common solutions for a cluster of ESFRI infrastructures in the field of "Life sciences"	
Deliverable title:	Progress of Compliance with Requirements of the Ethics Review Report	
WP No.	1	
Lead Beneficiary:	1: EMBL	
WP Title	Management	
Contractual delivery date:	30 June 2013	
Actual delivery date:	30 June 2013	
WP leader:	Janet Thornton	1: EMBL
Contributing partner(s):	n/a	

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Contents

1 Executive summary

The BioMedBridges project better enables researchers to access a wide range of data to facilitate new discoveries in health research and allows re-analysis of datasets, some of which will have been generated through rare, expensive or unrepeatable investigations, thereby ensuring maximum utility of these datasets. However, the sharing of data generated through the use of human material brings about ethical challenges concerning the protection of research participant privacy and confidentiality. To address this, a comprehensive ethical governance structure has been put in place, including an Ethical Governance Committee consisting of external experts that advises the project's Executive Steering Committee, and an Ethical Governance Framework document. In addition, to ensure compliance with the framework, the project is assisted by an Independent External Ethics Adviser. This report documents compliance with the ethical governance requirements.

2 Project objectives

With this deliverable, the project has reached or the deliverable has contributed to the following objectives:

No.	Objective	Yes	No
1	Manage the BioMedBridges project from Year 1-4		x
2	Organise the management meetings for all the project including: the Annual General Meeting for all partners; the Executive Steering Committee meetings (up to twice per annum) and the regular meetings of the Technical Coordination Committee (up to 3 times per annum)		x
3	Organise the Scientific Advisory Committee and their annual meeting, including reporting back to all partners		x
4	Provide good communication between all partners, through a professional web site		x

5	Ensure timely and appropriate reporting to the commission and completion of deliverables in all Work Packages		x
6	Develop metrics to assess the progress of the grant and its impact on the BMS community		x
7	Develop with all partners a plan for sustainability of the infrastructure built during the project, following completion of the grant		x
8	Ensure that ethics issues are addressed	x	

3 Detailed report on the deliverable

3.1 Bodies involved in BioMedBridges ethical governance

Apart from the Independent External Ethics Adviser (IEEA), the project calls upon the expertise of two of its committees when seeking guidance regarding potential ethical issues which may arise in the project. These two bodies are the Ethical Governance Committee (EGC) and the Executive Steering Committee (ESC). Amongst other duties, the EGC reports any ethics issues to the ESC and supports the IEEA. The ESC's duties include approving the project's Ethical Governance Framework.

3.2 BioMedBridges Ethical Governance Framework

The BioMedBridges Ethical Governance Framework (EGF) sets out policies for the project that relate to ethical and regulatory issues. It informs the ten Research Infrastructures (RIs) involved in the project, ensuring data is supplied and accessed within agreed terms.

The EGF highlights, in particular, considerations to be made with respect to national and international regulations, research participant consent, ethics

committee conditions of approval, trans-border/international access to data and linking data or types of data that were not linked before.

3.2.1 Ensuring data can be shared

The document states that data providers are responsible for all data made available, linked or accessed *via* the project, and must have obtained all appropriate approvals and consent required according to the laws and regulations in operation in the country in which they reside, including from ethics committees, data access committees and/or regulatory authorities or other bodies. It is clear in the EGF that deposition of data by data providers will act as assurance to the project that data providers have sought and obtained, where necessary, all appropriate approvals.

The majority of datasets will have been obtained before the initiation of the BioMedBridges project, and so the consent provided by the donors of these pre-collected samples may not have been broad and generic enough to cover the new uses to which the data will be put in the project, or for the sharing of data across national boundaries. If this is the case for a particular dataset, the project mandates—through the EGF document—that approval from an appropriate ethics committee and/or national authority, as required by law, must be sought prior to deposition of the data.

Re-consenting research participants may not be required if broad, generic consent has already been obtained, or an ethics committee or other appropriate national authority approves the use of the data without further consent and this is permissible according to national regulations. In this case, ethics committees will usually undertake a risk *versus* benefit analysis in order to reach a decision and may allow the research to go ahead without specific research participant consent, or they may decide that a different method of informing research participants is appropriate, such as putting the information about a new study in a newsletter or on a website.

The EGC was informed that some countries in the EU operate a legal ‘opt out’ system (rather than seeking consent) for the use of residual human tissue originally taken for medical purposes. In this case, any material surplus to

clinical requirements may be used in research without sample donor consent, unless that donor specifically requests the material is not to be used. The project agrees that if the opt out system allows for the sharing and use of the data in the ways defined by the project, data from these samples may be included in the project.

The project is aware that some researchers may seek a type of consent for future studies which allows research participants to retain control over their data, up until the point at which it is shared with other researchers or published. This would allow research participants to withdraw their data at any time up until this point.

At the second BioMedBridges Annual General Meeting in March 2014, some data providers explained that they would need to ask data requestors to supply additional information to prove they had approval to *use* particular datasets, which had not been foreseen in the Ethical Governance Framework. The project partners agreed that there may be additional requirements attached to the use of particular datasets, but it was up to the data providers to ensure that they were made known to data requestors. Some data providers also requested legally-binding data access agreements to be in place prior to sharing particular datasets. Once again, the project partners agreed that it was the data providers' responsibility to ensure that any agreements they deemed necessary in relation to their datasets were set up with data requestors as required.

Data providers making available any datasets for which there are underlying restrictions on use imposed by consent provisions, ethics committee or regulatory body requirements, legal agreements, time-limitations, or where there is an obligation to feedback findings of clinical significance, are mandated to complete a Data Provider Form on which they must list any restrictions or conditions.

The EGF makes reference to the use of data obtained *via* animal experimentation, and states that such data may only be used in the project if the research undertaken to generate it complies with the requirements of national and EU regulations, and was carried out under appropriate licences or

with other appropriate authority as relevant. Working within these requirements will ensure that due regard has been given to animal care and welfare.

3.2.2 Participant information and feedback of results

Although there is no plan to generate new data in the BioMedBridges project, the EGF makes it clear that research participant information sheets and consent forms to be used for new data collections should be drafted by the researchers or clinicians seeking consent. The project has provided template research participant information sheets and consent forms (see below) should the RIs require assistance in drafting these documents.

It is suggested that broad and generic consent for the use of datasets may better serve the purposes of the BioMedBridges project, and consideration should be given to consent of this type, along with an explanation to the research participant of any foreseeable risks—including an explanation that some risks may be unknown—and taking on board advice from ethics committees and national authorities where applicable. Information sheets should be drafted to cover the project's plans for access to and linkage of data stored in an electronic database, sharing of data across national boundaries, information about the management and communication of findings of clinical significance, and permission for future re-contact (if relevant). The EGF makes data providers aware that promising to destroy data after a certain time period is not practical if the data is to be used in the BioMedBridges project, as this data will need to be made available indefinitely, will be shared with other researchers, may be downloaded, and may be published.

In-line with any consent given, research participants may ask for their data to be withdrawn; however, it should be understood that the project cannot guarantee that any data already shared with other researchers or published will be removed, and prospective information sheets and consent forms should include a statement that explains this. It will not be possible to withdraw any unlinked anonymised data as this is no longer linked to research participant identifiers.

Direct feedback of research findings in the BioMedBridges project is not anticipated or planned, as the project is concerned with building data bridges and facilitating the sharing of datasets, rather than analysing data. However, data providers may have obligations to research participants to feedback some types of information, and they must inform data requestors of any obligations which reach through to them. Research participants must have consented to feedback and the mechanism for feedback should have been agreed with an ethics committee and/or national authority. There must also have been due consideration given to any predictive nature of the finding and how this impacts on the risk of a research participant succumbing to a particular disorder. It is known that individual perceptions of risk vary and this is compounded by the difficulty in assessing how the effects of a certain genetic variant may impact upon a particular individual, especially where other factors such as lifestyle and the environment may play a part. There are, of course, particular genetic variants for which the predicted risks to an individual are known, for example, BRCA1 genetic variance in relation to breast cancer risk, but there are many variants for which the risks are less clear. By bringing datasets together with other information, the BioMedBridges project may help to improve predictions of an individual's disease risk.

The EGF cautions against research findings which have not been validated to a diagnostic standard being fed back to participants. In addition, the project understands that open commitments to continuously re-evaluate data *ad infinitum* in order to feedback findings are not practical or sustainable, however, it does provide a Data Provider Form on which obligations to feedback findings should be noted.

3.2.3 Data ownership vs. custodianship

During the drafting of the EGF, there was a discussion amongst members of the EGC concerning ownership *versus* custodianship of data. It was determined that the term ownership implied holding the legal title and full property rights to one or more specific items of data, which would in turn imply that the 'owner' had the right or possibility, for example, to sell that data onwards or to destroy it, neither of which is the case. The study participant, the researcher, and the IT/data manager all have different rights and

responsibilities that cannot usefully be described as ‘ownership’. In contrast, custodians have legal rights and responsibilities which are transferable from one custodian to another; consequently, this was determined to be the more suitable term.

3.2.4 Data protection

The project makes clear that data providers have an obligation of confidentiality to research participants, and must conform to data protection principles to ensure that data are processed lawfully. Although the data used in the project will be anonymised (see discussion below), and no identifiable data will be shared, data held about a research participant may be unique—such as a person’s whole genome sequence—and if this is linked to other sources of data containing identifiable information, then the research participant may be identified[1]. The project acknowledges this risk, but can only ensure that datasets within its control are anonymised, and suggests that anyone combining datasets should consider any increased risk of identification that may arise as more and more pieces of information about an individual are brought together.

It is best practice to explain to research participants during the consent process the likelihood that they may be identified when research data is published, but it is difficult for researchers or clinicians seeking consent to foresee all uses to which research data may be put in the future, and to explain how datasets may be combined. It is better, therefore, to explain to research participants that the risk of identification may be considered to be minimal, but that the true risks are unknown and cannot be forecast. This will always be the case in research where technologies are progressing at a rapid pace, such as in DNA sequencing and analysis. If there is any doubt as to whether combining datasets may proceed, or whether consent provisions allow for the combination of datasets, the opinion of a relevant ethics committee or national authority should be sought regarding whether research participants should be contacted and additional consent sought for this activity.

[1] Gymrek et al. (2013) Identifying Personal Genomes by Surname Inference, Science http://dx.doi.org/10.1126/science.1229566

The document cautions against data analyses the results of which may unintentionally confer stigmatisation of subsets of populations. Where there may be potential for stigmatisation, publication of research results must be carefully considered and discussed with an ethics committee.

3.3 Audit of compliance with ethics requirements

From September to November 2014, the IEEA, together with the project manager, reviewed and conducted an audit of those parts of the project where sensitive data is handled or where there may be ELSI concerns. An interesting situation in WP8 resulted in more detailed follow-up and dicussion, the results of which are documented in Annex 4 to this document. Overall compliance with ethics requirements could be confirmed, with some areas needing additional attention as work progresses over the final year of the project.

3.4 Notes on ethical/legal discussions during project

The results of the following discussions were included in an updated version to the EGF as provided in Annex 1 to this document.

3.4.1 Defining anonymisation

There was some discussion on how anonymisation might be defined in the project. Although there is no internationally recognised definition and many terms abound, such as de-identified, linked anonymised, coded, pseudonymised, it was important to define the terms used in the project documentation so that all RIs understood what was meant by each term.

It was decided[2] that the term ‘anonymisation’ could be used to describe any data where identifiable information is not available to the researchers using the data. This term describes fully or unlinked anonymised data, but also linked, coded or pseudonymised data where the linkage key (code or cipher) is not held by, nor accessible to, the researchers/research establishment.

[2] Based on the recommendation by the Independent External Ethics Adviser and Irene Schluender, legal expert in WP5, TMF, Germany

Unlinked anonymised data contain no information that could reasonably allow anyone to identify the individuals to whom they relate, whereas linked anonymised (or coded or pseudonymised) data are anonymous to the researchers but contain information or codes that would allow others, such as a patient's clinician, to link them back to individuals.

3.4.2 Defining personal data

The important differences across countries in the EU regarding the definition of personal data were also discussed. In some EU jurisdictions, personal data may also be used to describe human biosamples since the information contained in the DNA within a biosample is unique to an individual and may be used to identify them. However, it was agreed that in BioMedBridges documentation, the term 'personal data' would refer to data which may be used to identify a research participant, such as name, address, National Insurance number, full postcode, and would not be applied to DNA sequence data.

3.4.3 Defining identifiable data

At the second BioMedBridges AGM, researchers involved in WP5 (Secure Access) requested a definition of identifiable data in order to help them construct their 'ethical and legal toolkit'. A list of possible identifiable data was drawn up based on the HIPAA list, but with the caveat that the combination of 'non-identifiable' data may produce a dataset that could lead to identification. It was discussed that considering what should be left out based on the potential consequences when data is combined was often more important than simply having a list of items that should not be included.

3.5 Template Research Participant Information Sheets and Consent Forms

Templates for adult and child research participant information sheets and adult consent and child assent forms (Annex 2 and 3) were drafted which RI partners might consider using. The templates were based on the UK's National Research Ethics Service (NRES) guidance, but are deemed suitable

for use throughout the EU. The child-friendly documents might potentially be used for adults who lack capacity if the reading level is deemed suitable. Each section of the adult information sheet has explanatory text which highlights the type of information that should appear at that point in the document. There is guidance attached to the templates which explains the rationale behind their drafting and how they might be used.

The templates will be made available via the BioMedBridges online tool to identify legal and ethical requirements as well as on the project website.

3.6 Overall assessment of the ethics provision for the BioMedBridges project

The IEEA determines that the ethical governance structure and framework, such as the EGC and EGF, are suitable for the project, and discussions have brought to light useful comments and debate about issues relating to the sharing of data across the EU. Although the governance provisions are restricted to the BioMedBridges project, it is hoped that some project partners will have benefited from the discussions and template documents produced, and these may be used to inform future ethics policies at these Research Infrastructures.

4 Delivery and schedule

The delivery is delayed: ☐ Yes ☑ No

5 Adjustments made

No adjustments were made.

6 Attachments

ANNEX 1. BioMedBridges Ethical Governance Framework, version 2.0

ANNEX 2. Template Adult Research Participant Information Sheet and Consent Form

ANNEX 3. Template Child Research Participant Information Sheet and Consent Form

ANNEX 4. Ethics Report Supplemental Document

7 Background information

This deliverable relates to WP1; background information on this WP as originally indicated in the description of work (DOW) is included below.

WP1 Title: Management
Lead: Janet Thornton, EMBL
Participants: all

The objectives of WP1 are the management of the BioMedBridges project, including organization of the management meetings such as the Annual General Meeting for all partners, the Executive Steering Committee meetings (up to twice per annum) and the regular meetings of the Technical Coordination Committee (up to 3 times per annum), and the meetings of the Scientific Advisory Committee, including reporting back to all partners. Among the tasks is also the provision of tools to ensure good communication between all partners, timely and appropriate reporting to the Commission and completion of deliverables in all Work Packages, development of metrics to assess the progress of the grant and its impact on the BMS community, the development of a plan for sustainability of the infrastructure built during the project and ensuring that any ethics issues that arise are addressed appropriately.

Work package number	WP1	**Start date or starting event:**	month 1
Work package title	Management		
Activity Type	MGT		

Participant number	1: EMBL	2: UOXF	3: KI	4: STFC	11: HMGU	13: VUMC
Person-months per participant	48	0	1	1	1	1

Objectives

1. To manage the BioMedBridges project from Year 1-4
2. To organise the management meetings for all the project including: the Annual General Meeting for all partners; the Executive Steering Committee meetings (up to twice per annum) and the regular meetings of the Technical Coordination Committee (up to 3 times per annum)
3. To organise the Scientific Advisory Committee and their annual meeting, including reporting back to all partners
4. To provide good communication between all partners, through a professional web site
5. To ensure timely and appropriate reporting to the commission and completion of deliverables in all Work Packages
6. To develop metrics to assess the progress of the grant and its impact on the BMS community
7. To develop with all partners a plan for sustainability of the infrastructure built during the project, following completion of the grant
8. To ensure that ethics issues are addressed

Description of work and role of participants

The project will be coordinated by Professor Janet Thornton at EMBL-EBI. The management structure will consist of an Executive Steering Committee, made up of the coordinators of the individual ESFRI BMS projects, and a Technical Coordination Committee, consisting of the Chairs and Co-chairs of the work packages. Janet Thornton will chair both committees. The Technical Coordination Committee will report to the Coordinator and Executive Steering Committee on a regular basis.

The tasks for this WP are as follows:

Task 1: Overall Coordination of the project The coordinator of BioMedBridges has full responsibility for managing this project and achieving its objectives, including infrastructure construction, project reporting and impact assessment and finance. The coordinator will be supported by a full time project manager, whose role will be to provide day-to-day support and implementation of all management and organisational tasks, including taking charge of accounting for

all financial aspects of the project. The project manager will be responsible for the content management of the web site.

An Executive Steering Committee, consisting of all the coordinators of the 10 BMS Infrastructures, which are contributing to this grant. This committee, which is chaired by the BioMedBridges coordinator (who also coordinates the ELIXIR infrastructure), will play a strategic role in the management of the project and be responsible for decisions on the financial management. They will measure progress against the specific objectives, milestones and deliverables of each work package, developing metrics to measure the impact of the work. They will also ensure good coordination with the members of their own the infrastructure. They will oversee the consolidation of the data-infrastructure needs of the different projects, and develop a joint policy on these issues. They will monitor the sustainability of the components of the infrastructure being developed and develop a plan for support following the completion of this grant. The Executive Board will meet twice in the first year: a kick-off meeting and an ordinary Board meeting. In subsequent years, there would be annual meetings, as well as conference calls every two to three months. It is anticipated that the meetings would be held in connection with the Annual General Meetings where possible.

The Technical Coordination Committee will comprise the coordinator of the grant and scientists in charge of different aspects of the construction work with responsibility for coordinating one work package (ie the chairs and co-chairs of the different construction Work Packages 1 - 5). The use case chairs will join this group as appropriate, during the tenure of their use case. This committee will therefore include technical experts taken from each infrastructure. This Committee has the responsibility to assess and report to the Executive Steering Committee on the progress of the work packages and to identify and prioritise future tasks for the following year. The chair for this committee will be the coordinator of the project. The Technical Coordination Committee will focus on the day-to-day and technical issues involved in achieving the planned deliverables and constructing the infrastructure. The Technical Coordination Committee will meet up to twice per year, in addition to the Annual General Meetings, and have monthly conference calls to deal with routine issues and resolve any urgent problems which may arise. The chairs and co-chairs of each Work Package will manage their own WP, ensuring good communication both within the WP and with the rest of this project, through this committee. This is described in more detail in the management section 2.1 below.

Task 2: Organisation of Management Meetings

The whole consortium will meet once a year at the Annual General Meetings.
This meeting will involve all the partners and those employed and working on the grant. Presentations will be made on progress on each work package and the use cases described. In the first year there will be an additional meeting at the start of the grant, to ensure good coordination from the beginning. The AGMs would also

be the main opportunity for the Executive Board and the Technical coordination Committee to meet and take joint decisions on the direction of the project, and for the advisory bodies (see below) to learn about the project and the progress being made, as well as providing strategic advice. The last AGM will be an open meeting, in part to provide outreach to all the members of each infrastructure, and also to ensure good uptake and exploitation of the deliverables of BioMedBridges. This meeting will be coordinated by WP2.

Task 3: Organisation of Scientific Advisory Board

The project will have two advisory bodies. We will construct a Scientific Advisory Board, which will comprise a small number of experts in the biological and biomedical life science infrastructure area. This will include world class biologists, IT experts, ethical and legal experts. In addition, representatives of the large e-infrastructures will be invited to form a Technology Watch e-Advisory Task Force, to keep the project informed on developments in this field and in general guarantee a close association between the ICT e-infrastructures and this project. The e-Advisory Task Force will form the Technology Watch Work Package (WP11), and consequently play a more integral part in the project than a conventional advisory board. It is anticipated that both advisory bodies would meet in connection with the Annual General Meetings.

Task 4: Provision of a professional web site

As well as providing the project with a public face, the project web site is also an important management tool. For this reason, the web site has been included in this work package, and will be based at EMBL-EBI, co-located with the coordinator and project manager. The internal/restricted part of the web site will be used both as a workplace and as a repository of documents. The task here is to provide the technical infrastructure for the website, whose contents will be controlled by the project manager.

Task 5: Reporting on the Project to Commission

The project coordinator will be responsible for reporting to the commission, with help from the project manager. Reports from each work package will be delivered by the chair of that work package to the project coordinator, who will then combine these reports to deliver a coordinated report.

Task 6: Developing and monitoring progress and impact

The management bodies will develop procedures and metrics at the beginning of the grant to measure the progress of the grant and its impact on the biological and medical research communities. These metrics will be reported annually. All the partners involved in this WP will have responsibility for this task.

Task 7: Developing Sustainability Plan

During the course of the project the executive steering committee will monitor the sustainability of the infrastructure under construction. All the partners involved in this WP will have responsibility for this task. In the last year of the project the executive steering Committee will report on the long term sustainability of each component delivered.

Task 8: Establish an Ethical Governance Committee

The Ethical Governance Committee will:

- provide an ethics management report to each meeting of BioMedBridges Executive Steering Committee
- Analyse the requirements from the Ethics Review Report
- Review the draft Ethical Governance Framework document
- Monitor the compliance of the project beneficiaries with the Ethical Governance Framework
- Prepare new versions of the Ethical Governance Framework for approval by the Executive Steering Committee
- Support the External Independent Ethics Advisor in the preparation of Progress of Compliance with Ethics Requirements Reports.

Subcontracting for Audit Certificates: EMBL (Partner 1), STFC (Partner 4), UDUS (Partner 5), TUM-MED (Partner 7), TMF (Partner 10), HMGU (Partner 11), VUMC (Partner 13), UH (Partner 16).

Deliverables

No.	Name	Due month
D1.1	Website	12
D1.2	Devise metrics to measure progress and impact of construction	12
D1.3	1st Periodic Report	18
D1.4	2nd Periodic Report	36
D1.5	Final Report & Sustainability Plan	48
D1.6	ED1: The Ethical Governance Framework for BioMedBridges	18
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D1.8	ED3: External Independent Ethics Advisors Report	48

BioMedBridges

Ethical Governance Framework

Version 2, October 2014

Contents

Definition of terms used in this document

Anonymisation

Data are considered to be anonymised where they are fully (unlinked) anonymised or linked (coded, pseudo-) anonymised where the linkage code (cipher) is not held by, or accessible to, the researchers/research establishment.

Anonymised – also known as 'unidentified' in some EU Member State's national legislation. The sample or data does not contain information identifying a person, or the link to such information has been permanently severed. Anonymised data do not contain any identifiable information such as, for example, name, address, phone number, full date of birth, national health or social insurance numbers, full postcode, etc., and it is not reasonably possible for the researcher to identify the individual to whom the data relate.

Pseudonymised – also known as 'coded' or 'linked'. The sample or data is connected to a person, but this connection has been marked with an identifier that does not contain information identifying that person. Pseudonymised data contain information or codes that would allow certain individuals (e.g., the clinical team who collected them or an independent body entrusted with the safekeeping of the code) to link them back to identifiable individuals.

Personal Data – Data which may be used to identify a research participant. In the EU, this includes pseudonymised data, although some exemptions to certain requirements which apply to personal data, such as data subject access, will apply in this case. (Note: Although in some EU jurisdictions, personal data may also be used to describe human biosamples, in the context of this template, it relates to identifiable data only).

Data

The term 'data' in this document may refer to genomic data, anonymised images, metadata, etc. It does not refer to data that contains identifiable information such as name, phone number, or date of birth.

Data provider

The ‘data provider’ is the individual researcher or investigator or body of researchers or investigators that makes data available for access and use within the BioMedBridges project. (It does not refer to the participant.)

Participants

The term ‘participant’ refers to an individual whose data are accessed within the scope of the BioMedBridges project. Participant in this document is equal to “data subject” in applicable EU legal documentation.

Ethics committee

The term ‘ethics committee’ in this document refers to a committee which has given ethical approval for a study which has collected data that will be subsequently made available by the data provider within the BioMedBridges project. (It does not refer to the BioMedBridges Ethical Governance Committee.)

Project

‘Project’ refers to the BioMedBridges project (funded by the European Commission within Research Infrastructures of the FP7 Capacities Specific Programme, grant agreement number 284209).

Project coordinator

‘Project coordinator’ refers to the European Bioinformatics Institute, which coordinates the BioMedBridges grant.

Research Infrastructures

The ten Research Infrastructures (RIs) involved in the BioMedBridges project include:

- Biobanking and Biomolecular Resources research infrastructure (BBMRI)
- European Advanced Translational Research infrastructure in Medicine (EATRIS)

- European Clinical Research Infrastructures Network (ECRIN)
- European Life Science infrastructure for Biological Information (ELIXIR)
- European Marine Biological Resource Centre (EMBRC)
- European Infrastructure of Open Screening Platforms for Chemical biology (EU-OPENSCREEN)
- European Biomedical imaging infrastructure (Euro-BioImaging)
- European Research insfrast4ructure on Highly Pathogenic Agents (ERINHA)
- European Infrastructure for Phenotyping and Archiving of Model Mammalian Genomes (Infrafrontier)
- Integrated Structural Biology Infrastructure for Europe (INSTRUCT).

1 Introduction

1.1 Project aims

This document sets out policies for the BioMedBridges project that specifically relate to ethical and regulatory issues with regard to the storage and access of data.

The objective of the BioMedBridges project is to better enable researchers to access data, increasing its utility with the ultimate goal of benefiting society, for example by facilitating new discoveries in health research and by allowing re-analysis of expensive, rare or unrepeatable investigations, while continuing to protect the interests of research participants with regard to their privacy and confidentiality.

1.2 Background for the Ethical Governance Framework

The aim of this Ethical Governance Framework is to enable the BioMedBridges project to operate within agreed terms with respect to participant consent, ethics committee approvals and national regulations, ensuring researchers supply and access data whilst working under a common ethical framework. The framework has been written so that very different datasets can be utilised in an

ethically-coherent manner to maximise research benefit, while acknowledging the responsibilities and obligations that are owed to research participants.

Data providers have a number of responsibilities and obligations, such as the obligation to respect participant confidentiality. Researchers accessing the data have a custodian role, to ensure the careful and responsible management of the information. They have an obligation to operate in conformity with the requirements of their own institution, and fulfil all necessary national and international regulatory and ethical requirements. They also have obligations to the BioMedBridges project, as well as the funders and the wider research community, to carry out high quality, ethical research.

The purpose of this document is to provide a framework for the project and to focus on specific issues that are key to the development and operation of BioMedBridges. To achieve this, ethical policy documents established by other large-scale consortium projects, including the Wellcome Trust Sanger Institute's UK10K project, have been drawn upon during the writing of this framework.

1.3 Background of the Research Infrastructures involved in the project

Concerning the issues involved in data security and ethical governance of the BioMedBridges project, it is essential to define the roles and responsibilities of the ten biomedical sciences research infrastructures (RIs) involved in the project:

1. RI that hold and/or provide data (e.g. Infrafrontier, Elixir, ECRIN)
2. RI that provide only metadata (e.g. BBMRI)
3. RI that have no data or are users/consumers of data (e.g. ECRIN, EATRIS).

Data security and full consideration of ethical issues are not only relevant to RIs that hold data, but are also the responsibility of all RIs that intend to use the data.

1.4 Project-specific considerations

Consideration should be given for handling data within the project with respect to

- Trans-border/international access to data
- Establishment of new links between data or types of data that were not linked before.

2 Project bodies involved in ethical governance

The bodies involved in ethical governance of the project are:

- The Independent External Ethics Advisor
- The Ethical Governance Committee, which is comprised of experts whose backgrounds cover the different areas of the project
- The Executive Steering Committee.

2.1 Independent External Ethics Advisor

The Independent External Ethics Advisor:

1. Monitors and reports on the progress of compliance with requirements of the Ethics Review Report and reports on this to the Commission *via* Periodic Reports
2. Oversees the development and preparation and implementation of the Ethical Governance Framework
3. Advises the Ethical Governance Committee, the Executive Steering Committee and the project coordinator on all ethical issues
4. In consultation with the Ethical Governance Committee and the project coordinator, ensures that the project operates to appropriate ethical standards.

2.2 Ethical Governance Committee

The Ethical Governance Committee:

1. Monitors the compliance of the project beneficiaries with the Ethical Governance Framework
2. Provides an ethics management report to each meeting of the BioMedBridges Executive Steering Committee (every three months)
3. Supports the External Independent Ethics Advisor in monitoring and reporting on the progress of compliance with the requirements of the Ethics Review Report and Ethical Governance Framework
4. As necessary, prepares updates of the Ethical Governance Framework, to be approved by the project's Executive Steering Committee.

2.3 Executive Steering Committee

The Executive Steering Committee:

1. Is responsible to ensure that there is no scope-creep within the project with respect to unforeseen use of the mechanisms, processes and infrastructure developed during the project to facilitate the transfer and use of data where Ethical, Legal and Social Issues (ELSI) pertain
2. Approves the Ethical Governance Framework and any updates thereof
3. Ensures that suitably qualified individuals are appointed for the role of Independent External Ethics Advisor and the Ethical Governance Committee.

3 General provisions

3.1 Regulatory approvals

Responsibility for all data that is made available, linked or accessed via the services provided by the project remains with the data providers and must have been obtained in accordance with the laws and regulations in operation in the country in which the data provider resides. This includes any requirement for approval from an appropriate ethics committee or other regulatory body.

Depending on the type of consent given by the participant, there may be joint data custody between the participant and the data provider. It is the responsibility of the data provider to ensure that such joint custody is not in conflict with the provisions of this framework and that the data may be used within the project.

Data providers should determine whether, with respect to the use in the project, any additional approvals may be required for the data they have collected.

Where data providers have collected data from participants in countries outside of their own (another data 'source country'), they must ensure that approvals have been given by appropriate ethics committees and/or other regulatory bodies in the source country of the data to be used in the project.

Data obtained *via* the use of animals in research can only be made available for the BioMedBridges project if the work has taken place within the requirements of national regulations and with appropriate licences or authority permission as required by national law, and with due consideration given to animal welfare and care.

3.2 Documentation

For datasets where there are underlying restrictions on use, data providers must certify using the form provided in Appendix 1 to this document that they will abide by this Ethical Governance Framework and its stipulations, and that appropriate ethical approval and/or consent are in place prior to use of the data within the project.

The data provider forms will be collected by the project coordinator and stored centrally.

3.3 Updates to the framework

As the project evolves, adjustments may be made to this framework. Any adjustments shall be developed and agreed by the Ethical Governance Committee and approved by the Executive Steering Committee.

4 Human participants

4.1 Data providers

The project has been designed to enable maximal benefit from research by making data as accessible as possible to the research community, while protecting the interests of participants from whom the data originate with regard to their privacy and confidentiality, and within the scope of their consent.

Data providers are responsible to ensure that the responsible ethics committees, data access committees, national regulatory authorities or equivalent bodies have granted approval for the data they provide to be accessed within the project. The data provider must ensure that prior approval is available before any deposition of data which may be accessed by users of BioMedBridges services occurs. The project is aware that different EU Member States impose different requirements as regards the necessity for research participant consent or ethics committee approval when samples are taken for therapeutic or diagnostic purposes, and are then subsequently used in research.[1] Data providers must ensure any requirements have been met and appropriate approvals obtained. Deposition of data by the data providers will act as assurance to the project that data providers have sought and obtained, where necessary, all appropriate approvals as required by relevant national laws and regulations. Where there are underlying restrictions on use of a particular dataset in the project, the data provider form included in Appendix I to

[1] For example, the Act on the Medical Use of Human Organs, Tissues and Cells (Finland), allows tissues originally taken for diagnostic purposes to be used for medical research with permission from the health care unit, as long as no personal data are used. However, in England, Wales and Northern Ireland, the Human Tissue Act stipulates that this use would require research participant consent if samples of 'relevant material' were taken from the deceased and National Research Ethics Service (NRES) research ethics committee approval if samples were taken from the living without consent for research - even if the samples were anonymous to the researchers or pseudonymised. The same requirement applies in England, Wales and Northern Ireland, where DNA analysis is to be undertaken on anonymised or pseudonymised biological material from the living without research participant consent.

this document must be completed and submitted to the project coordinator. Where there is any doubt, or where the consent does not foresee the use of data in BioMedBridges, approval from an appropriate ethics committee or national authority as required by law or regulation must be sought before data are deposited for use in the BioMedBridges project.

4.2 Confidentiality and data security

All data providers have an obligation of confidentiality and must conform to data protection principles to ensure that data is processed lawfully.

In some areas of the project, the level of detail of data held on a participant may be such that it will be unique to that participant and thus, if linked to other non-anonymised data, could potentially be used to identify the participant. This raises important privacy protection issues. As such, data held within the project must always be anonymised or pseudonymised. Consequently, identification by a third party would only be possible if extra information for a participant were to be made available; for example, if another dataset was available elsewhere containing data associated with the participant's name, and this was in turn used in conjunction with data that is made available within the project.

Certain data analyses may confer non-intentional stigmatisation of subsets of the population involved. Consequently, any new study within the project that may have the potential to cause stigmatisation through the publication of the results of analyses must be carefully considered and discussed with an appropriate ethics committee in order to obtain further guidance prior to the analyses being undertaken.

4.3 Informed consent

Where the project involves the use of patient data, prime consideration should be given to whether existing consent for the use of this data in the project is sufficient and in accordance with any requirements set down in national guidelines or protocols, which may be upheld by relevant national or local authorities, or by ethical or regulatory bodies. This includes consent given by participants residing in a source country that is different from the country the data is subsequently deposited in. Where this was not initially consented, the

responsible authority or research ethics committee should approve the sharing of data across national boundaries. However, in the case of countries using a legal 'opt out' system relating to the use in research of participants' residual human tissue originally taken for medical purposes, rather than a consent process, data from these samples may be included in the project if the 'opt out' system allows for the use and sharing of the data in ways defined by the BioMedBridges project.

Novel ways of combining data or datasets within the project can proceed as long as data is anonymised or pseudonymised and an appropriate ethics committee or national authority has granted approval where required. Where there is doubt that consent provisions adequately cover the combination of datasets, the opinion of an appropriate ethics committee or national authority should be sought as to whether additional participant consent is required.

4.3.1 Adequate consent available

Where pre-collected participant consent adequately covers the use of data in the project, no further consent will need to be sought.

4.3.2 Adequate consent not available

Where adequate consent has not been obtained, or where there is doubt, a data provider should seek approval from an appropriate ethics committee and, where national requirements dictate, from a relevant regulatory body or authority, before the data can be deposited. An example for this may be pre-collected data where consent or approval was not broad enough to include the use of the data in BioMedBridges.

4.3.3 Consent forms

Drafting consent forms and obtaining consent for new data collections is entirely the responsibility of the researcher collecting the data, and the responsibility to ensure that appropriate consent and/or ethics committee or other authority approval is in place before data is deposited and/or made available for the project lies exclusively with the data provider.

It is suggested that, going forward, broad and generic consent[2] for the use of datasets may better serve the purposes of the BioMedBridges project, and that consent of this type should be considered, along with advice from appropriate ethics committees and national authorities, where applicable.

It is also suggested that, for future studies and trials, consent should allow for participants to retain control over their data so as to allow for withdrawal up until the data is shared with other researchers or published.

Consent forms should be drafted to adequately cover the BioMedBridges project plans for:

- Access to and linkage of data that is stored in an electronic database
- Sharing of data with other researchers within and outside of the country
- Any decisions made regarding the management and communication of findings of individual clinical significance, including any obligations data consumers may have to communicate findings, and any pre-set time-limits for the feeding-back of results
- Permission for future re-contact (if needed).

When drafting consent forms and participant information sheets, it should be ensured that the provisions in these documents do not preclude data sharing, such as by promising to destroy data unnecessarily.

Re-consent

Re-consent is not required if a broad consent has been obtained, nor if an appropriate ethics committee or relevant authority agrees that the benefit of using the participant's data in the project outweighs any risk to that participant, and local, regional or national regulations allow authorities or ethics committees to make this decision.[2] Ethics committees may decide on alternative methods of informing participants of the uses to which their data may be put, for example, by sending a letter by recorded delivery to the participant's home if they have agreed to be re-contacted, and giving the participant the option to

[2] Note that in some members states legislation may determine when broad consent may be used, for example, the Finnish Biobank Act stipulates that broad consent for use of human biological samples and associated data may only be used in the context of a biobank.

withdraw data that relates to them if not integrated in a dataset or published. Newsletters and websites can also serve as communication tools.

4.4 Feedback to participants

In general, direct feedback of results and incidental findings within the project to participants is not anticipated or planned. The project is concerned with building data bridges, constructing tools and technology to link up different types of data, not with processing and analysing data. Provisions surrounding feedback of results and incidental findings directly to participants are thus unnecessary and beyond the scope of the project.

Data providers should inform the project coordinator via the data provider form (Appendix 1) if they, or any third party who uses the data, are under any obligation to communicate (feedback) findings of individual clinical significance to participants.

The mechanism of feedback must have been consented to by the participant, agreed with an appropriate ethics committee or national authority and findings must be validated to a diagnostic standard prior to reporting back to the participant. Conversely, participants should be informed during the consent process if no feedback will occur. However, it must be understood before a dataset is used for the project that an open commitment to re-evaluate ad infinitum data from a participant to identify clinically significant findings is not sustainable and, if feedback is considered, there must be an unambiguously predictive relationship between the finding and the disease.

4.5 Participant withdrawal

Due to the nature of the project, although data may be removed if a participant withdraws their consent, it will be impossible to guarantee the complete withdrawal of individual data from all researchers who have already accessed it.

Where possible, the data held on a participant who wants to withdraw will be removed; however, it will not be possible to remove anonymised data. If there is any doubt that participant consent might not allow for the retention of data

under the circumstances detailed above, then advice from the responsible ethics committee or national authority should be sought prior to making the data available within the project.

5 Use of animal data

Where the project involves animal data, the data provider must ensure that national guidelines for their welfare and care during collection of the data were followed.

Animal life must have been respected and research work to collect data undertaken within the requirements of national regulations and with appropriate licences or permission by the responsible authorities as required by national law.

6 Assurances to third parties

Assurances made to third parties, such as those found in Material Transfer Agreements, must be included with any accompanying information sent with a dataset prior to its inclusion in the project. If these assurances include any restrictions on the use of a dataset in the project, the data provider form at Appendix I must be completed and sent to the project coordinator.

7 Time-limited data

Data providers must make any information about time-limitations attached to datasets by virtue of consent restrictions, ethics committee approval or national regulations, available to the project administration by completion of the relevant section on the data provider form.

BioMedBridges

Data provider form

This form must be completed by all parties providing data where there are underlying restrictions on use imposed by consent requirements, ethics committee approvals, national regulations or any other agreements within the BioMedBridges project

NOTE: Custody of all data made available within the project remains with the provider (and, where applicable, the participants). The data provider has full responsibility for the data when making it available within the project under the terms agreed within the BioMedBridges Ethical Governance Framework.

1	Name of data provider	
2	Name and address of data providers' research institute/university	
3	Name of dataset and URL of dataset or service	
4	Please list the restrictions on use imposed by consent requirements, ethics committee approvals, national regulations or any agreements, such as, research collaboration agreements, material transfer agreements, and data access agreements, including those made with other parties who may have originally supplied the data	
5	Is the research participant data anonymised* or pseudonymised?	
6	If pseudonymised, name the person(s) holding the linkage key	
7	If pseudonymised, please give the name and address of the linkage key holder's research institute/university	

8	If applicable, please state if there is a date by when this dataset must be removed from BioMedBridges	
9	Please state any decisions made regarding the management and communication of findings of individual clinical significance, including any obligations data requestors may have to communicate findings, and any pre-set time-limits for the feeding-back of results	
10	Please sign to indicate that you have read the BioMedBridges Ethical Governance Framework document and you agree to abide by the conditions contained therein	
11	Please sign to confirm that the donor consent provisions and/or ethical approval, and national laws and regulations, allow the use of the data in BioMedBridges *If you are unsure whether the current consent provisions or ethical approval adequately allow the use of the data in BioMedBridges, we recommend you seek advice from an appropriate ethics committee*	
	For Office Use Only	
	Signature of BioMedBridges Coordinator representative	
	Date of approval	

∗ See definitions in the BioMedBridges Ethical Governance Framework document

Template:
Information Sheet and Consent Form

Definitions

In this document, the following definitions apply:

Anonymised – also known as 'unidentified' in some Member State's national legislation. The sample or data does not contain information identifying a person, or the link to such information has been permanently severed.

Pseudonymised – also known as 'coded'. The sample or data is connected to a person, but this connection has been marked with an identifier that does not contain information identifying that person.

Biobank – Any biosample repository or archive that is used for research purposes.

Biosample – Any human biological material, including extracted DNA/RNA samples.

Personal Data – Data which may be used to identify a research participant. (Note: Although in some EU jurisdictions, personal data may also be used to describe human biosamples, in the context of this template, it relates to identifiable data only).

How to use this template

This template is made to help gain research participant consent for the use of human biosamples and/or personal data in cases where the initial consent given by the research participant/data subject at the time of the collection of the material/data did not cover the now intended use.

First and overall importance: Asking for further consent assumes that the donor of the biosample(s) and/or data in question has given his/her prior consent to be contacted again by the institution now seeking further consent to use the biosample(s)/data. This consent to be contacted is a necessary prerequisite to using this template. If this requirement is not met, it would be a breach of privacy to use the research participant's contact details in order to seek consent to further use of the biosample(s)/data.

Secondly, valid consent to the use of personal data and human biosamples requires that the following conditions have been met:

- Consent must be freely given and informed.

- Potential donors must consider whether the decision may affect any present or future health care or entail any other disadvantages.
- Information is provided about the intended use(s) of the biosample(s)/data, including any rights of the donor, e.g., to withdraw the given consent at any time.
- The Information Sheet provided should be a visible part of the consent declaration in order to underline that the participant has been properly informed before signing the declaration.

Informed consent could explicitly indicate a specified research purpose and this specification can be a challenge for biomedical research and even more for biobanks. Research purpose can, without doubt, be properly specified in cases where the use of biosample(s)/data is limited to one single study with a clearly defined study purpose outlined in a study protocol. Beyond this, it is widely recognised that consent for a broader research purpose, such as studies concerning a certain disease, is sufficient. The concept of 'broad consent', e.g., consent for any medical research study, which would be most helpful for research in cases relating to the use of human biosample(s)/data from biobanks, is gaining ground within the EU in cases where the aim of the biobank cannot be limited to research into specific diseases. In some EU member states it is not the prevailing view and is not considered the most informative form of consent, or is legally restricted only to samples in biobanks. It is, therefore, recommended that, where known, any future research purposes should be explained to the research participant as precisely as possible. Alternatively, the general aim of the biobank should be indicated in a clear manner.

The highest level of anonymisation should be used, whenever possible, to protect research participant's privacy. It should also be noted that anonymised data are not considered to be personal data under Data Protection legislation and that anonymisation requires proper de-identification in the sense that the research participant/data subject is not identifiable by reasonable means. However, full (unlinked) anonymisation deprives the donor of his/her right to withdraw his consent and claim the remaining material. Therefore, for this reason, data protection agencies are beginning to recommend that full anonymisation should be avoided.

Constant technical developments challenge the concept of anonymisation of biosample(s) which may contain genomic DNA sequence, and whole genome sequencing is getting more and more feasible and affordable. Detailed genetic data, especially whole genome sequence data, is unique to one person and, as such, any risk of re-identification should be explained.

Incidental findings regarding undetected health risks or diseases of the donor raise the question of whether there is an obligation to inform the donor. On the other hand, any 'right not to know' must be respected. This conflict cannot completely be resolved but should, at least, be duly managed through implementing an explicit declaration explaining what will happen regarding the feedback of incidental findings to the sample donor.

In order to take into account varying research purposes and remaining legal uncertainties, the consent declaration template is generic. As discussed above, the validity of broad consent may be invalid under certain jurisdictions or in the future. However, considering the fact that the concept of broad consent for medical research is gaining ground, it is recommended to collect broad consent to make future use of the biosample(s)/data possible. It is however important to ensure that the current intended use is covered by the scope of the consent under present applicable law.

At this stage, open access to or publication of the full genome of a human being requires specific, unambiguous consent and is not included in this consent form.

Notwithstanding the validity of broad consent, the future uses of the biosamples and data have to be specified as precisely as possible and great care should be taken to ensure that

the information provided is correct and complete - otherwise there is a risk that the consent does not cover the intended use.

Please note, that this suggested template information sheet and consent form will have to be assessed and adapted to the aim of the biobank and/or database using it. The template document eventually used must be in-line with advice from appropriate ethics committees and national authorities, where applicable.

The information sheet should provide clear information on the essential elements of the research, the voluntary nature of involvement, what will happen to the research participant, the potential risks/inconvenience balanced against any possible benefits.

Information About the Research

This section is to ask the potential participant to consider taking part in the research.

Invitation to take part

You are being invited to take part in a major medical research project carried out by the "XXXBiobank/research establishment(s)" [fill in official name of legal entity that is authorised to enter into this agreement]. Before you decide whether to join, it is important for you to understand why the research is being done and what it would involve for you. Please take the time to read the following information carefully, and discuss it with us and others if you wish.

If anything is not clear, or if you would like more information, please telephone XXX to talk to a member of the project team. More information about XXXBiobank/research establishment is also available at www.XXXbiobank.xx. At the assessment/screening visit, there will be a further opportunity to ask any questions that you might have.

Thank you for taking the time to consider taking part in XXXBiobank/research study.

Biobank/research establishment contact details:… [fill in contact details]

What is the purpose of the XXXBiobank/Research?

Purpose is an important consideration for research participants and should be presented clearly, succinctly, and in context.

[Adapt, if necessary:] The purpose of this biobank/research is to improve the prevention, diagnosis and treatment of a wide range of illnesses (cancer, heart disease, diabetes, dementia) and joint problems and to promote health throughout society. By analysing answers, measurements, samples and health data collected from sample donors/data subjects, researchers may be able to work out why some people develop particular diseases while others do not. They may also detect unknown diseases and new genetic defects. Thus progressive research objectives may emerge in the future and your biosample(s) and/or personal data and/or anonymised data may be used for research purposes which, at this stage, are unknown. This research should help us find new ways to prevent early death and disability from many different diseases.

XXXBiobank/research is not intended to directly help those who give their consent for their biosample(s) and/or personal and/or anonymised data to be used – but research may give future generations a much better chance of living their lives free of diseases that may disable and even kill.

Why have you been invited to take part in this research?

This section should explain why and how the participant was invited or recruited.

You were identified through your participation in [fill in name of project where the biosample(s)/data have been collected] research project where you gave consent to be contacted again in the case when your sample(s) might be needed for research projects beyond the scope of your original consent. The only information used, in confidence, to contact you is your name and address. We do not know anything else about you, and have not seen any of your medical records.

Do you have to take part?

It should be explained that taking part in the research is entirely voluntary.

No, it is up to you to decide to join the research. We will describe the research and, if you agree to take part, we will then ask you to sign a consent form. You are free to withdraw your consent at any time, without giving a reason.

What will you have to do?

This section may not be appropriate when asking research participants to re-consent. However, we have included guidance here in case this is the first time participants are being consented for a study.

In this section, it should be clear exactly what will happen and what you will expect of your research participants. This section should include how long the participant will be involved in the research, how long the research will last, if and how often the research participant will need to meet a researcher or visit the biobank/research establishment, how long these visits will last and what procedures will be carried out. Specific mention of any video/audio-taping or photography should be made. Specific mention will be needed if published material will identify the subject.

[Adapt, if necessary:] You will be invited to attend XXXBiobank/research establishment/place for a screening visit at which time we will ask you questions about your health. We will then take a blood sample (3 teaspoonsful) and ask you to spit into a small sample tube.

Expenses and payments

This section may not be appropriate when research participants are being re-consented. However, if used, this section should explain if expenses, e.g., travel, are available and consideration should be given to detailing here information about any vouchers given as a 'thank you' for participation.

How will your sample be stored?

Details about how the samples will be stored should be detailed, including how long they may be stored for, if stored in anonymised or identifiable form, provision for destruction, where and if the samples may be shared with others.

Your sample will be stored under [optional: state which applies] a pseudonym (linked or coded anonymised), or will be fully (unlinked) anonymised if you consent to full anonymisation. [Optional: Additional text for pseudonymised samples] In the case of pseudonymisation of samples, any personal, identifiable data will be kept separately from your sample(s) and controlled by different persons in order to impede re-identification.

Biosamples and/or data may be stored indefinitely, that is, they may never be destroyed and will be shared with many researchers around the world for multiple studies.

How will personal, identifiable data be kept confidential?

This section should explain who will have access to personal, identifiable data and how research participant confidentiality will be safeguarded. How procedures for handling, processing, storage and destruction of data match appropriate legislation may be included.

We will follow applicable ethical and legal practice. Access to research participants' personal, identifiable data is restricted within XXXBiobank/research establishment, and all staff sign confidentiality agreements as part of their employment contracts. Data or samples provided to researchers will be anonymised and will not include personal, identifying details. This should prevent identifiable information from being used – inadvertently or deliberately – for any purpose other than to support research. Computer security to block unauthorised access (for example, by "hackers") to the computers that hold personal information, is installed.

Although research studies may require the sequencing of your whole genome (your DNA), this sequence data will not be published in its entirety and made accessible to researchers

unless you specifically consent to making the data openly accessible. In some research studies, whole sequence data will be made accessible to other researchers through a 'managed access' system, which ensures that the data is only accessed by genuine researchers who agree not to try and identify the person from whom the sample came. However, in the case of managed access studies, you will still need to give consent to the publication and sharing of your whole genome sequence data.

Why do we need your written consent?

This section should explain that consent is voluntary and that by signing a consent form the research participant is confirming that they are willing to donate a biosample and/or data to research.

Your donation of your biosample(s) and/or personal data to XXX Biobank/research establishment is entirely voluntary. By signing the consent form, you are confirming your willingness to donate.

Can you withdraw your consent?

This section should explain what the research participant can and can't expect if he or she withdraws his or her consent. The position on retention/destruction of data/samples upon withdrawal of consent must be made clear. It may not be possible for all data to be extracted and destroyed.

You will be free to withdraw your consent and to ask for your sample(s) to be destroyed at any time without justification, unless the sample(s) has been fully (unlinked) anonymised. In the case of withdrawal of consent, your sample(s) will be destroyed and your personal data deleted except where any fully anonymised samples and/or data have already been shared with researchers.

Will your sample and/or data be shared with or transferred to other biobanks or databases?

Details should be given concerning any plans for the sharing of samples and/or data. As much information as possible should be given to the research participant about any potential uses to which their samples and/or data may be put.

The XXXBiobank/research establishment is taking part in the European research project called [fill in]. We are establishing 'databridges' to increase the power of our research by sharing linked (coded) or fully anonymised data with other researchers who may combine these data with their own datasets. The aim is to [fill in]. Therefore we need to [fill in extent and kind of possible sample/data exchange]. Your sample(s)/data will be handled within this

research under equivalent data protection and confidentiality safeguards in order to ensure your privacy. The exchange will not affect your right to withdraw your consent (see above).

What are the possible disadvantages and risks of taking part?

The risks of participation should be explained. Any risk, discomfort or inconvenience should be outlined. Consider carefully how to explain risk in research. Consider insurance issues and whether patients should be informed that their participation may affect insurance cover. Any risk of incidental findings should be explained.

Before participating, you should consider if this will affect any insurance you have and seek advice, if necessary.

Any collection, storage and transfer of data concerning your biosample or genetic information involves the general risk of re-identification in the future due to the constant progress in re-identification techniques and the continuing increase of publicly available information. Although minimal, these risks cannot completely be excluded. The risk would increase, for example, if you make further genetic information available, e.g., for genealogy purposes. XXXBiobank/research establishment will o take all appropriate measures to protect your privacy and to share and transfer your personal data to researchers who can assure us that they will store the data under appropriate data protection and confidentiality safeguards in order to ensure your privacy, and agree not to try and re-identify sample/data donors.

What are the possible benefits of taking part?

Any benefits of taking part in research should be explained but, where there is no intended benefit, this should be stated clearly. It is important not to exaggerate the possible benefits.

We will not be feeding back any results from the research to you but, although you will not benefit directly from the research, the information obtained may help improve the treatment of people who suffer from diseases and health disorders.

What if there is a problem?

Any complaint about the way you have been dealt with or any possible harm you might suffer will be addressed. If you have a concern about any aspect of the research, you should ask to speak to the researchers who will do their best to answer your questions. Please contact XXXname, XXXphone and XXXemail address. If you remain unhappy and wish to complain formally, you can do this by [*insert details*]. The XXXBiobank/research establishment has appropriate insurance/indemnity in place and, in the event that something does go wrong

and you are harmed during the research, then you may have grounds for a legal action for compensation – but you may have to pay your legal costs.

Involvement of the General Practitioner/Family Doctor

It should be explained if the research participant's family doctor or other health care practitioner needs to be notified of their participation, and consent should be sought for this. An explanation should be given of what information might be exchanged.

We will not be telling your family doctor of your involvement in this research.

What will happen to the results of the research study?

Participants often want to know the results of a study they have been in, but it may not be possible to provide this information. Broad scientific results of a research study and results relevant to an individual should be considered and will need to be managed differently. Research participants should be told what will happen to the results of the research and whether results will be published or made publicly accessible in another way.

The results of the research will be published. Linked (coded, pseudo-) and unlinked anonymised data may be placed into research databases and accessed by many researchers, but they must assure us that they will store the data under appropriate data protection and confidentiality safeguards in order to ensure your privacy, and agree not to try and re-identify research participants.

Who is organising and funding the research?

The organisation, charity or company sponsoring the research should be explained. Any conflicts of interest should be declared.

XXX is funding this research. [Adapt:] XXX will be paid for including you in this study.

Who has reviewed the study?

Give details of any ethics/biobank steering/governance committee approvals that are required.

The research study has been reviewed by a group of people called a research ethics committee, to protect your interests. This research has been reviewed by XXX and given a favourable opinion.

Further information and contact details

The research participant should be given an appropriate contact point for general information about the research and to whom they can approach if unhappy about any aspects.

For further information about this research you should contact XXX. If you are unhappy about the research and wish to complain, you should contact XXX.

You will be given a copy of this information sheet and your signed consent form to keep.

Thank you for considering taking part in this research.

Declaration of consent

The research participant is consenting to everything described in the text of the information sheet. For some studies an itemised or hierarchical consent form may be needed especially if the study includes consent to use of audio/video-taping, with possible use of verbatim quotation or use of photographs; transfer of data/samples to countries with less data protection than the EU; agreement to receive individual feedback. The signatories to the consent should be the research participant and the person taking consent. An independent witness is not routinely required except in the case of consent by a research participant who may be blind, illiterate, etc.

Title of Research:

Name of Researcher:

Thank you for reading the Information Sheet and for asking any questions that you might have had. If you would like to participate in the research, please respond to each of the following questions by writing your initials in the boxes and then signing the form.

The following sample(s) have been taken:… [fill in any biosample stored, e.g. blood sample, tissue etc.]

The following data will be derived from your sample(s): … [fill in, in particular when genome sequencing is intended]

The following data have been collected: ... [fill in any personal data stored]

Please initial each box

1. I confirm that I have read and understand the information sheet dated [date] and have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my consent is voluntary and that I am free to withdraw at any time without giving any reason and without my legal rights being affected. ☐

3. I hereby agree that the biorepository (name and full contact details) has the right to use and further transfer to other biobanks/databases, and research establishments around the world, the sample(s) and/or personal data as indicated in the information sheet. ☐

4. I give permission for long-term storage and use of my biosample(s) and/or my personal data as indicated in the information sheet for this purpose. The usage of data comprises indefinite storage in an electronic data base and linkage to other research data. ☐

5. [Optional for fully anonymised samples]
I understand that my sample(s) will be used for many different research purposes and that withdrawal of consent and subsequent destruction of the sample is excluded in the case of fully anonymised transfer. ☐

6. I hereby agree that the XXXBiobank/research establishment may contact me at any time in the future in order to ask me for further cooperation in sample(s) and/or personal data donation. My contact details may be stored exclusively for this purpose and will not be disclosed to any third party. ☐

7. I understand that no incidental findings will be given to me and that I will not benefit financially from taking part (e.g. if research leads to commercial development of a new treatment). ☐

Name of sample donor/data subject	Date	Signature of sample donor/data subject
Name of legal representative in case of minor or legally incapacitated donor	Date	Signature of legal representative in case of minor or legally incapacitated donor

Name of person taking consent	Date	Signature of person taking consent

When completed: 1 for research participant; 1 for biobank/researcher's file

Template:
Children's Information Sheet and Assent Form

How to use this template

Please refer to the BioMedBridges Information Sheet Template to be used for adults for these details and for guidance about each of the sections in this document.

This template may also be used for adults who lack capacity if it is assessed to be of the correct reading level.

Note to researchers:

It is always helpful to add some illustrations to the information sheet and assent form to help children understand and make the document more attractive to them.

This template should be used as a general guide and many ethics committees will wish to see different information sheets and assent forms for different age ranges, for example, 3 to 6 years old, 6 to 12 years old and 12 to 16 years old.

What is a research study?

Research studies help us learn new things. This paper talks about our research and the choice that you have to take part in it. We want you to ask us any questions that you have. You can ask questions any time.

Important things to know:

- You get to decide if you want to take part in this research.
- You can say 'No' or you can say 'Yes'.
- No one will be upset if you say 'No'.
- If you say 'Yes', you can always say 'No' later.
- You can say 'No' at anytime.

Information About the Research

Invitation to join in

- You are being invited to join a big research project at a place called "XXXBiobank/research establishment(s)" [Note to researchers: This may need simplifying.].

- Research means doing work to find out about things, and this research is finding out about things which might affect people's health, such as illnesses.

- It is your choice to decide to participate or not. Before you decide whether you would like to join in this research, it is important for you to understand why the work is being done and what you will have to do.

- You can either read this paper or, if you prefer, an adult can read this form with you. You can ask questions any questions you want while you read the form. You could also chat about it with us and your parents if you wish.

- If you don't understand anything, please ask your Mum or Dad to telephone XXX to talk to us. If they want to, your Mum or Dad can go onto the internet at look at the work we do at www.XXXbiobank.xx. If you would like to join in, when you come to see us you can ask lots more questions.

What is this research?

[Adapt, if necessary:] At this biobank/in our research we do work which might help doctors find out why some people get ill, how to stop them from becoming ill and how to make them better again.

We would like to take some blood and spit from you. These are called 'samples'. The work will take a long time and so we will keep your samples for a long time and use them in work which we might not yet know we need to do.

We will not be able to tell you what we have found in our research, but your sample will help us understand things about why some people get ill.

[Optional] Why have we asked you to help us in our work?

Your samples were used by other scientists doing research and you or your parents agreed that it was OK to talk to you again about this new work.

What will you have to do?

[Adapt, if necessary:] You will come to XXXBiobank/research establishment/place for a visit and we will ask you some questions. We will then use a small needle to take some blood from your arm (3 teaspoonsful) and we will ask you to spit into a small tube.

The poke with a needle to test your blood can hurt. We can put a cream on your skin before we take blood. This cream would help so it won't hurt as much.

You can say 'no' to what we ask you to do for the research at any time and we will stop.

Will you share my sample with other scientists?

Yes. Other scientists around the world might want to use your samples in their work. If we do give other scientists your samples though, we will not be able to get them back and you need to understand this.

Your name will be secret

Your blood and spit (samples) will be stored under a made-up name or a number so no-one will know they came from you. Any information about who you are will be kept separate from your samples, so no-one will be able to work out that you gave the samples. We might never throw your samples away, and we might share them with many other scientists so they can use them in their own work.

How can you decide whether or not to join in?

You can choose if you want to give us a sample. By writing your name on the form you are saying you are happy to join in, but you can change your mind at any time.

Can I say I don't want to join in anymore?

Yes. You can tell us at any time that you do not want to be part of our work anymore. No-one will ask you why and no-one will be upset with you. We might not be able to throw your samples away, but you will not be asked to come back or join in anymore.

We will also not be able to get your samples back from other scientists we have sent them to.

What might be good and what might be bad about joining in?

As we might share your samples with other scientists, some people might try to work out who you are, but it will be very difficult for them to do this.

How will my samples help you?

We will not be able to give you any information we find out from our work, but we can tell you that your samples might help us find out why some people get ill and we might be able to help people get well again.

What if I am not happy?

If you are not happy with how things went when you came to us to give your samples, you must speak to your parents or to a member of our research team. Your parents will then be able to phone us on XXXphone or email us at XXXemail address.

What will you do when you do your work and find some things out?

We will write up our work and send it to scientific magazines so that other scientists will be able to read about our work. We might put our results into something called a 'database' which other scientists can look at.

Can I ask more questions?

Yes. You can ask your parents to get in touch with XXX. You will be given a copy of this paper and your signed form to keep. Thank you for thinking about joining in!

Is there anything else?

If you want to be in the research after we talk, please write your name below. We will write our name too. This shows we talked about the research and that you want to take part.

If you don't want to be in the study, you don't have to be.

It is also OK to say yes and change your mind later. You can stop being in the research at any time. If you want to stop, please tell the research team or your parents.

Declaration of assent

Title of Research:

Name of Researcher:

		Please write the first letter of your name in each box if the sentence is true
1.	I have read, or someone has read to me, the paper dated 11th July 2014 and I have asked questions.	
2.	I understand that I do not have to join in and I can change my mind at any time.	
3.	I am happy that my samples might be sent to other scientists around the world to use in their work.	
4.	I am happy that my samples might never be thrown away.	
5.	I am happy for the scientists at XXXBiobank/research establishment to ask my parents if I would like to join in another study.	
6.	I understand that I will not get any information about the work the scientists do with my samples and that I will not	

get any money for joining in.

Name of sample donor/data subject	Date	Signature of sample donor/data subject
Name of legal representative in case of minor or legally incapacitated donor	Date	Signature of legal representative in case of minor or legally incapacitated donor
Name of person taking consent	Date	Signature of person taking consent

When completed: 1 for research participant; 1 for biobank/researcher's file

Annex 4: Legal basis for sharing of personalised medicine data across borders: WP8 case study

Background

In preparation of the report, the project's IEEA, Carol Smee, and the Project Manager, Stephanie Suhr, carried out a review of compliance with the Ethical Governance Framework (EGF) across all BioMedBridges work packages (WPs). Preliminary analysis of the data showed that only one work package (WP), the WP8 Use Case Personalised Medicine, had data for which a BioMedBridges Data Provider Form[1] would need to be completed.

On closer inspection of the data in question, which is used for research by the WP8 lead at the Finnish Institute for Molecular Medicine, specific issues were raised regarding how sharing of data might be achieved while ensuring compliance with the requirements of the EGF. It was decided that the data to be used within WP8 would form an interesting case study in the IEEA report, highlighting possible difficulties with proposals to share data across national borders even within the European Union.

The following questions regarding the WP8 dataset revealed some interesting and significant considerations, which we discuss here:

- Would it be possible to share the dataset outside of the Finnish institute that obtained the original samples? If not, why not?
- Is deposition of this dataset in public repositories planned?
- How is access to/use of the dataset regulated?
- What does the information sheet provided to research participants state concerning the sharing of data?

[1] As per the BioMedBridges Ethical Governance Framework, this form must be completed by all parties providing data, where there are underlying restrictions on use imposed by consent requirements, ethics committee approvals, national regulations or any other agreements within the BioMedBridges project. See http://www.biomedbridges.eu/sites/biomedbridges.eu/files/documents/deliverables/biomedbridges_ethical_governance_framework_v1-2.pdf

Definition of “biobanks” in Finland

Following discussions with the WP8 lead, it transpired that there is a significant difference in the way the term ‘biobank’ is understood in Finland compared to for example the UK, including how a biobank might operate and for what purposes researchers might be able to use samples deposited there. Looking at the Finnish Biobank Act[2], the conditions for establishing a biobank (Section 6) ask for a description of the biobank’s area(s) of research and restrictions concerning the use of samples. For example, if the area of research of a biobank is “haematology”, the use of samples would be restricted to research into haematological disorders. In contrast, the general understanding in the UK is that a biobank is a collection of samples that may be used for many different areas of research, although some restrictions may apply to some collections.

Consent and use of samples

In Finland, research participants now provide two different types of consent for the use of their samples: (1) for (a) specific research project(s) with restrictions on further/other use and, (2) for biobanking of their samples, if appropriate and desired by the research participant. If type (1) consent is in place, additional specific consent for any other project would need to be obtained even if type (2) consent has been given in conjunction with depositing samples in a biobank, if the scope of the new project falls outside the biobank’s area of research and that of the original study. Consents for older sample collections may have been generic in the past, and so the use of samples from these studies may not be as restricted. However, samples collected for specific projects in the past may still be transferred by the sample collection ‘owner’ to a biobank as long as the sample donors are informed of the transfer and are given the opportunity to opt out. No response from the sample donor to information regarding the transfer may be taken as an agreement to the transfer.

[2] http://www.finlex.fi/fi/laki/kaannokset/2012/en20120688.pdf

Use of DATA associated with samples

Information as to how to deal with data is less clear in the Finnish Biobank Act, as data is only mentioned *in connection with* samples, that is, as 'samples and information associated with them'. However, interpretation suggests that no automatic access to data (linked to samples) can be granted, and sharing can only occur where consent is in place for that sharing. For the specific case in WP8, the information on the website of the responsible biobank (FHRB)[3] suggests that samples (and linked data) are coded/linked anonymised (coded samples are deposited at FIMM while the key to identifying the patient stays at the hospital). In summary, it is assumed that data associated with coded/pseudonymised samples where consent is in place for a specific research project can only be used for work within that project. This appears to rule out sharing of the pseudonymised data linked to samples within BioMedBridges WP8, unless new consent is obtained for sharing, or the original consent was broad enough to allow this to happen. Sharing of data associated with samples held in a biobank is possible for studies undertaking work within the biobank's area(s) of research when samples are also requested. It is not clear in the Finnish legislation whether pseudonymised data can be 'untangled' from the samples they are associated with, and subsequently used and shared for general research purposes.

Obtaining permission to use samples or data

Applications made by researchers to biobank steering committees for access to data require a description of the research project and information about the duration of the study. The biobank maintains control over how the samples it stores will be used and by whom. This same principle would of course be very difficult to uphold in the case of data that is made widely available for research as is planned within BioMedBridges. However, it appears that the Explanatory Notes that accompany the Finnish Biobank Act do not place the same restrictions on the data generated and subsequent results of analyses produced by researchers accessing the samples. They may return such data to the biobank, which continually updates information about the samples and

[3] http://hematology.fi/fhrb

associated clinical data and may also receive follow-up samples from the same research participants. However, there is an issue in that the biobank in question may not be able to store complex genetic data in a user-friendly way.

Basis for use of WP8 data in BioMedBridges

In any EU country, identifiable data can only be used under the terms of applicable data protection legislation, and the Finnish Biobank Act does set specific requirements concerning the use of identifiable or coded/pseudonymised samples. It does not, however, appear to cover the use of unlinked (fully) anonymised samples. As there is no specific description of procedures for the use of only data (without samples) in the Finnish Biobank Act, interpreting this legislation as it applies to use and sharing of data alone, as opposed to use and sharing of “samples and associated information”, is problematic. However, the Finnish data protection legislation does not apply to unlinked anonymised information. Therefore, in case of the BioMedBridges project, the applicable Finnish legislation *does* appear to allow the use of *unlinked* anonymised samples and associated data without (new, specific) consent, and this will include sharing of data across international borders. It also seems that, if DNA sequencing was carried out using pseudonymised biobank samples, the researchers would be at liberty to publish or share the sequence data without restriction, including in public databases as long as it was anonymised, as there does not appear to be a restriction placed on the data subsequently generated by researchers accessing biobank samples. Use of unlinked anonymised samples in studies appear to afford the researcher freedom to publish and share data generated by the use of those samples, but this does bring with it the considerable and important ethical issue that fully anonymised samples and any associated data cannot be removed from sample collections – even if sample donors wish to withdraw their consent.