ADOPT BBMRI-ERIC
GRANT AGREEMENT NO. 676550

DELIVERABLE REPORT

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Deliverable Title	Ethical Governance Framework and Ethics Check for ADOPT BBMRI-ERIC
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ETHICAL GOVERNANCE FRAMEWORK

Executive Summary

The aim of this Ethical Governance Framework is to enable any future project members of BBMRI-ERIC 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 draft framework presented below has been written on the basis of other EU funded projects works[1] in order to ensure reliability and consistency of the systems in place, with the concern that very different samples and 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.

[1] Namely the BioMedBridges - FP7 Project GA n°284209 Deliverable on BioMedBridges Ethical Governance Framework ; CAGEKID, Cancer Genomics of the Kidney - FP7 Project GA n° 241669 , Deliverable 8.4; ESGI, European Sequencing and Genomics Infrastructure - FP7 Project GA n°262055, Deliverable 7.5 and 7.7.

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Document log

Issue	Date (yyyy-mm-dd)	Comment	Author/partner
D5.7	2016-09-30	M12	Anne Cambon-Thomsen
D5.7_Rev1	2017-11-12	During the mid-term review "minor issues to the deliverable" have been noted by the reviewer requesting revision on - Deposition of samples – how? - Non-intentional stigmatization of subjects – clarify/examples - IC – how to help users determine if consent is sufficient - How implementation is accelerated The updates will be made as requested. The updates also include lessons-learned from the colon-cancer case study and other case studies.	Michaela Th. Mayrhofer

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ADOPT BBMRI-ERIC gateway for health

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This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under grant agreement No 676550.

1. Background

The aim of this Ethical Governance Framework is to enable future members of BBMRI-ERIC to operate within agreed terms with respect to the participant consent, ethics committee approvals and national regulations, ensuring researchers supply and access data whilst working under a common ethical framework.

2. Approaches (Methods)

The draft Ethical Governance Framework (see Appendix) was written on the basis of other EU funded projects[2] and in liaison with the EU Project CORBEL[3] that comprises of and networks among the BMS RIs. This especially, in order to ensure reliability and consistency of the systems in place. It builds on the previous work of the EU Project BioMedBridges[1].

The Governance Framework aims at giving an orientation on ethical issues to be taken into account in a transnational project setting where samples and/or data are exchanged. The Ethical Governance Framework was developed within BioMedBridges for data and updated within ADOPT BBMRI-ERIC and CORBEL to address samples and/or data.

Additionally, BBMRI-ERIC developed an ethics check (modelled on the EU FP7/H2020 of the Ethics Unit for the specific purpose of addressing issues of sample and/or data exchange. The ethics check is primarily intended as a service tool for researchers to help them assess if they have considered all ethical considerations appropriately.

3. Results

Based on the request for revision by the mid-term reviewer, the following adaptions/clarifications have been made to the Ethical Governance Framework:

1. *Deposition of samples and/or data*

The paragraph has been adapted in the Ethical Governance Framework to clarify the that informing the coordinator on the status of approvals is critical in order to ascertain that the appropriate approvals are indeed in place. It now reads as follows (adaption in bold):

> "Deposition of samples and/or data by the providers **may** act as assurance that samples and/or data providers have sought and obtained, where necessary, all appropriate approvals

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

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as required by relevant national laws and regulations. Where approvals are necessary, the provider **has to** inform the project coordinator **on the status of approvals."**

2. *Non-intentional stigmatisation*

"Certain data analyses may confer non-intentional stigmatisation of subsets of the population involved." A new study on old datasets has the potential to cause stigmatisation. If a risk, this must be raised to the ethics committee.

3. *Informed Consent and Data Protection Breaches*

Whether current consent is deemed sufficient or re-consent is required is ultimately an issue to determine by the competent national/local research ethics committee, not BBMRI-ERIC. Additionally, the *BBMRI-ERIC Access and Sharing Policy* (approved by the AoM on November 8th 2017, draft version relates to D4.1) specifies that "requesters and providers are expected to take the necessary precautions and safeguards to avoid subjects' privacy breaches. This entails protecting their personal data and putting in place state-of-the-art safety measures for data security." To this policy, BBMRI-ERIC partners/users adhere to. Audits on that matter are not possible from the BBMRI-ERIC side, however, ensuring appropriate education and training and awareness raising are.

4. *Accelerate Implementation*

The Governance Framework and esp. *Ethics Check* are field-tested in the context of the colon cancer case study of ADOPT BBMRI-ERIC. The assessment is still ongoing but has already lead to the development of a workflow diagram (see Figure 1) to highlight the service character of the Ethics Check for researchers. The BBMRI-ERIC Ethics Check is intended as a service for biobankers, national/local ethics committees and researchers when research requires samples and/or data from biobanks in multiple countries. Procedure A is intended as a self-help tool for researchers to assess if all ethical issues are met. BBMRI-ERIC will require proof that all ethical reviews are in order. If requested, the ELSI Helpdesk Coordinator might assist. Procedure B is only relevant if there is no competent research ethics committee. In this case, an ad-hoc committee might be formed (details see Appendix). This review might also provide a service to research ethics committees to assess the project in question (possibility discussed and interest detected with members of national ethics committees). in their decision making. Ultimately, it is always the biobank that decides to grant access & provide samples/data.

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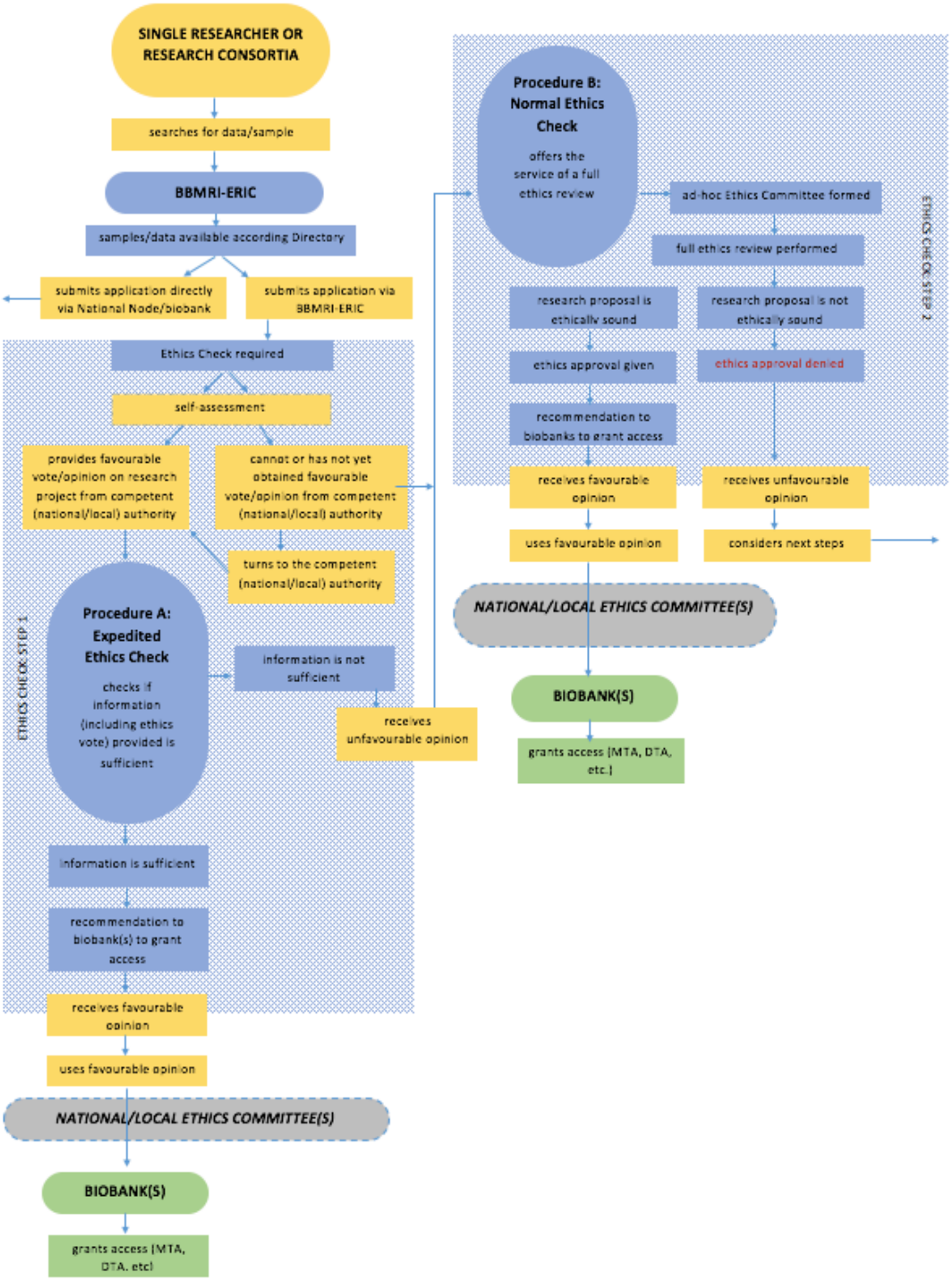
Figure 1: Ethics Check Procedure A and B

Legend: *Yellow: single researcher or research consortia**;** Blue: BBMRI-ERIC**;** Green: biobank**;** Grey: National/local Ethics Committee*



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4. Discussion and Conclusions

The Ethical Governance Framework has been updated. The ethics check is still field-tested in the context of the colon cancer case study of ADOPT BBMRI-ERIC (results are expected when the colon cancer case study is completed). This may lead to further adaptions in the suggested framework prior to implementation within the research infrastructure BBMRI-ERIC. So far, the testing has shown that the ethics check was perceived by researchers as an extra burden as regards to ethical review. Improving with the process flow chart has led to the change of perception that it consists a service. In the context of sample/data exchange within ADOPT BBMRI-ERIC it informs the contractual agreements between data providers, controllers.

5. Next Steps

After final field tests and adaptions, the ethics check will become a publicly available service of BBMRI-ERIC Common Service ELSI. It has to be advertised as a service to research ethics commitees, researchers, biobankers and within BBMRI-ERIC. A close collaboration with CS IT is necessary to make it as user friendly (potentially online-tool) as possible.

6. References

BBMRI-ERIC Access Policy and Procedure (Draft version D4.1), final version approved by the Assembly of Members in its session on 8 November 2017.

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Appendix I – Ethical Governance Framework

Project-specific considerations

Consideration should be given for providing ELSI support for handling samples and/or data within the project with respect to

- Trans-border/international access to samples and/or data for research uses (inside the EU and with non-EU countries)
- Establishment of new links between data or types of data that were not linked before.
- Existing ELSI tools or services provided by the scientific community

Bodies involved in ethical governance

The bodies involved in ethical governance of the project are:

- The Independent **External Ethics Advisor**
    - 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
    - Oversees the development and preparation and implementation of the Ethical Governance Framework
    - Advises the Ethical Governance Committee, the Executive Steering Committee and the project coordinator on all ethical issues
    - In consultation with the Ethical Governance Committee and the project coordinator, ensures that the project operates to appropriate ethical standards.
- The **Ethical Governance Committee**, which is comprised of experts whose backgrounds cover the different areas of the project
    - Monitors the compliance of the project beneficiaries with the Ethical Governance Framework

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- Provides an ethics management report to each meeting of the BioMedBridges Executive Steering Committee (every three months)
- 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
- As necessary, prepares updates of the Ethical Governance Framework, to be approved by the project's Executive Steering Committee.

- The Executive **Steering Committee**
  - 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 samples and/or data where Ethical, Legal and Social Issues (ELSI) pertain
  - Approves the Ethical Governance Framework and any updates thereof
  - Ensures that suitably qualified individuals are appointed for the role of Independent External Ethics Advisor and the Ethical Governance Committee.

General Provisions of the Ethical Governance Framework

Regulatory approvals

Responsibility for all samples and/or data that are made available, linked or accessed via the services provided by the BMS RIs remains with the samples and/or data providers and must have been obtained in accordance with the laws and regulations in operation in the country in which the 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 more or less potentiality for using the samples and/or data for research purposes. It is the responsibility of the samples and/or data provider to ensure that the uses of the resources are not in conflict with the provisions of this framework and that they may be used within the project.

Samples and/or data providers should determine whether, with respect to the use and the purposes of the project, any additional approvals or procedures are required for the biological resources (samples and data) they have collected.

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Where providers have collected samples and/or data from participants in countries outside of their own (another '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 biological resource to be used in the project.

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

Updates to the framework

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

Human participants

Samples and/or data providers

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

Samples and/or 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 biological resources they provide to be accessed and used within the respective project. The provider must ensure that prior approval is available before any deposition of samples and/or data which may be accessed by users of BMS RIs services occurs.

Deposition of samples and/or data by the providers may act as assurance that samples and/or data providers have sought and obtained, where necessary, all appropriate approvals as required by relevant national laws and regulations. Where approvals are necessary, the provider has to inform the project coordinator on the status of approvals.

Once samples are collected for research, the principal investigators shall fulfil the role of custodians of the samples, to ensure the careful and responsible management of the samples and information entrusted to their care by research participants. The obligations are transferred to a new custodian who must ensure the original obligations to research participants are honored.

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Confidentiality and data security

All samples and/or data providers have an obligation of confidentiality and must conform to data protection principles to ensure that data, and particularly sensitive personal data (e.g. health, genetic, biometric data) is processed lawfully and in the respect of applicable best practices.

In some areas, 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, personal data held within the project must always bede-identified to the extent possible in order to fulfil the research purpose. Consequently, identification by a third party should only be possible if extra information for a participant were to be made available.

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.

Informed consent

Where the project involves the use of personal 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 project.

Novel ways of combining data or datasets within the project can proceed as long as data is linked or unlinked anonymised 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

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ethics committee or national authority should be sought as to whether additional participant consent is required.

Adequate consent available: Where pre-collected participant consent adequately covers the use of samples and/or data in the project, no further consent will need to be sought.

Adequate consent not available: Where adequate consent has not been obtained, re-consent must be sought, if national law does not provide for exceptions.

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 for the use of samples and/or datasets may better serve the purposes of the BMS RIs, and that consent of this type should be considered, along with advice from appropriate ethics committees and national authorities, where applicable.

Consent forms should be drafted to adequately cover the BMS RIs plans for:

- Access to and linkage of samples and/or data stored
- Sharing of samples and/or 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 through adequate communication process, and any pre-set time-limits for the feeding-back of results
- Permission for future recontact
- Instructions how to handle withdrawals.

Re-consent

Re-consent is not required if a valid broad consent has been obtained, Ethics committees may decide on alternative methods of informing participants of the uses to which their samples and/or 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 withdraw samples and/or personal data that relates to them. Newsletters and websites can also serve as communication tools.

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Feedback to participate

The ELSI support intends to encourage and positively support projects' leaders in the design of fitted procedures to return selected incidental findings that would result from their research activities using samples and/or data, this being notably done through the Ethics Check procedure described below. In general, it is not scarce that feedback of results and incidental findings within the project to participants is not anticipated or planned. Projects' leaders as well as samples and data providers should inform the project coordinator if they, or any third party who uses the samples and/or data, are under any obligation to communicate (feedback) incidental 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 sample set or dataset is used for the project that an open commitment to re-evaluate ad infinitum samples and/or 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.

Feedback of incidental findings to research participants is only ethically justified if the analytical validity, the clinical validity and the clinical utility of those findings are previously established in an independent manner.

Participant withdrawal

Research participation is voluntary: research participants thus retain a right to discontinue their participation to the study at any time.

Personal data held on a participant who wants to withdraw will be removed or fully anonymised.

Use of animal samples and/or data

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

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Animal life and welfare 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.

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.

Time-limited materials

Samples and/or data providers must make any information about time-limitations attached to the materials made available by virtue of consent restrictions, ethics committee approval or national regulations, available to the BMS RIs and project responsible persons by any means.

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ETHICS CHECK

Ethics check will be set for projects to a simple and efficient procedure to check the protocols presented by applicants for both the scientific merit of their project and their adherence to principles and practices of ethically acceptable research. The Ethics Check procedure is building on the work of the Common Service ELSI of BBMRI-ERIC and it is integral part of the ADOPT BBMRI-ERIC project's Ethical Governance Framework. It shall enable the partners to operate within agreed terms with respect to participant consent, ethics committee approvals and national regulations ensuring researchers supply and access data and/or samples whilst working under a common ethical framework. The Ethics Check is trialed in the context of ADOPT and shall henceforth become a corner stone of BBMRI-ERIC and its ethical and legal framework.

The Ethics Check is an analysis of ethical, legal and social implications of research projects or programs regarding the International and European applicable laws, ethical principles and relevant best practices, in accordance with a specified list of considerations established in this document.

It is a verification of the presence/absence of the necessary evidence of respect of International and European relevant laws for the research activity that will be performed, and of the necessary elements that will be useful for National competent ethics committees or other authorities that have to approve the project according to the National framework.

The Ethics Check is an add-on process and a service for researchers that articulates with existing ethical reviews mechanisms at National and European levels without constituting neither disproportionate nor unnecessary administrative burdens for projects' leaders. The Ethics Check does not aim to substitute the authority of competent research ethics committees at national, regional, local levels to be consulted according to applicable national laws. It also does not aim to duplicate ethic committee approvals where already granted.

Below is described the Ethics Check Criteria for Common Service ELSI (p. 9-22), and the operational procedure (p. 23-26).

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BBMRI-ERIC COMMON SERVICE ELSI ETHICS CHECK CRITERIA (DRAFT)

Object of the document

This document specifies the criteria for the BBMRI-ERIC Common Service ELSI (here-after the CS ELSI) independent Ethics Check of research projects and programmes.
This activity necessitates establishing objective and systematic criteria to be used in the Ethics Check:

- For deciding which project/program necessitates an Ethics Check (cf. point 1)
- For performing the Ethics Check (cf. point 2 and 3)

The criteria set up in this document are based on already existing criteria used by the European Commission in the context of the EU research and technological development framework programmes such as H2020.

Scope and purpose of the ethics check

The Ethics Check is a precondition in order to be allowed to use the resources of BBMRI-ERIC identified through the BBMRI-ERIC Directory 2.0.
The Ethics Check is an analysis of ethical, legal and social implications of research projects or programs regarding the International and European applicable laws, ethical principles and relevant best practices, in accordance with a specified list of considerations established in this document.
It is a verification of the presence/absence of the necessary evidence of respect of International and European relevant laws for the research activity that will be performed, and of the necessary elements that will be useful for National competent ethics committees or other authorities that have to approve the project according to the National framework.
The Ethics Check is an add-on process that articulates with existing ethical reviews mechanisms at National and European levels without constituting disproportionate nor unnecessary administrative burdens for projects' leaders. The Ethics Check does not aim to substitute the authority of competent research ethics committees at national, regional, local levels to be consulted according to applicable national laws.
In the context of the procedure A described below (cf. point 2), the Ethics Check allows BBMRI-ERIC to ensure that the access and the provision of any support from the BBMRI-ERIC is only allowed for research projects presenting sufficient legal and ethical guarantees. Additionally, in the context of the procedure B described below (cf. point 2),

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the Ethics Check may facilitate the works of national competent ethical review committees by checking minimal criteria of European and International ethical-legal compliance.
Therefore, the opinion from the BBMRI-ERIC Common Service ELSI Ethics Check has no mandatory implication for these competent committees according to national laws, nor to authorities involved to review the project/programme within the concerned ERIC Member States.
Complementary document: Ethics Check Operational procedure. Available on the intranet.

Criteria and procedures of the ethics check

1- Ethics check implementation criteria

This step aims to check the eligibility of the demand and is ensured by the CS ELSI Secretariat, at the time of receipt of the application.

Eligibility criteria:

Research projects or programs subject to an Ethics Check must:

- have a transnational feature by involving the use of resources from several National Nodes AND
- include European or international samples and data flows
  AND
- consist of a non-interventional or observational research involving the reuse of existing human samples, biofluids or micro-organisms maintained in biobanks that are part of BBMRI-ERIC.

An Ethics Check shall systematically be implemented as a part of the decision-making process in case of a request from a research promoter for BBMRI-ERIC support as defined here-below:

- access requests to the European biological resources managed by National Nodes' members, OR
- funding applications of research projects involving BBMRI-ERIC budget, OR
- projects/programmes requesting the ethics management to the CS ELSI, OR
- access requests to technical Common Services and capacities offered by the ERIC.

Exclusion criteria:

Any project that is out of the scope of the above-defined implementation criteria are not subject to the Ethics Check. This should not damage their right to participate to

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BBMRI-ERIC activities in the respect of other procedures and requirements, nor to participate to, or benefit from, other services offered by the CS ELSI.

Due to the specific scope of BBMRI-ERIC activities, the Ethics Check:

- does not apply to animals' biological resources
- does not apply to clinical research
- does not apply where the research promoter is subjected to the H2020 ethical review. However, in such a case, the CS ELSI can be asked for advice in the preparation of the ethics part, in order to meet the European Commission requirements or answer to recommendations.

2- Ethics check procedures

The applicant (research promoter) to the access to BBMRI-ERIC support(s) must transmit the scientific part and the ethics part of his/her project to the CS ELSI for the purpose of the Ethics Check. If necessary, any complementary information could be requested by the CS ELSI experts involved. All the information will be processed in the respect of professional secrecy and confidentiality.

Two alternative procedures have to be used according to the state of development of the project regarding ethical/legal/social implications.

- **Procedure A: Expedited Ethics Check**

The applicant has already gathered all nationally competent ethics committees' approval and other relevant authorisations to perform the research in accordance with the respective law.
In this case, the applicant has just to fulfill **step 1 below (self-assessment)**.
Regarding step 1 in this procedure "A", the expert group shall check whether:

1. All relevant information has been answered/provided (*Completeness of the information*)

2. The right information is provided (*Truthfulness of the information*)

3. The relevant approvals / authorisations related to the envisaged activities are well referenced (*Appropriateness of the information*)

A **formal statement** signed by the research promoter stating that all the necessary approvals/authorisations to begin the research have been obtained can be requested and recorded into the applicant dossier maintained by the Common Service ELSI.

- **Procedure B: Normal Ethics Check**

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The applicant has not gathered all the necessary ethics approvals and authorisations to perform the research.
Exceptionally, where the applicant justifies the impossibility to access to any Ethics Committee in his/her country to get approval of the project/program but that these activities are submitted to an Ethics Check in application of the criteria set up in this document, the procedure B must be followed and the opinion given by the BBMRI-ERIC Common Service could have a broader scope in terms of ethico-legal compliance regarding relevant enforceable international frameworks.
In these cases, the applicant is subject to **step 1 and 2 below (self-assessment + checking criteria)**.
Regarding step 2 and procedure "B", the expert group shall check deeper whether:

1. All relevant information has been answered/provided (*Completeness of the information*)

2. There is no contradictory information (*Truthfulness of the information*)

3. Given answers and related documentation are of quality and comply with applicable framework. If necessary experts can take action to be reported to the applicant if a particular answer is problematic; e.g. pointing out lack of information, inconsistencies, compliance issues or irregularities (*Appropriateness of the information*)

3- Steps and criteria

STEP 1: Self-assessment (Procedure A and B)

For any application satisfying the inclusion criteria defined above (point 1), the applicant is invited to fulfill the following self-assessment table in order to allow preparing the Ethics Check of the planned research activities.
This step intends to identify activities and ethical issues that shall be considered by the experts.
The applicant shall appropriately tick the corresponding boxes (items) in the following grid and specify further where necessary or requested.

Item 1: SCIENTIFIC GOALS, EXPECTED OUTCOMES AND BBMRI-ERIC SUPPORT(S)	
Which are the research aims?	*Please, briefly describe the purpose(s) of the research and page where there is further description.*

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Which are the expected benefits for individuals and the society?	*Please, briefly explain the function of the expected research outcomes.*		
What kind of support(s) from BBMRI-ERIC is requested? *BBMRI-ERIC support includes any financial, technical, intellectual supports provided by the ERIC, including through its Common Services or from at least 3 National Nodes.*	*Please, describe and link with the purposes of the research*		
Item 2: ORIGINS OF THE BIOLOGICAL RESOURCES (SAMPLES/DATA)	YES/NO		Fill in as appropriate
Does this research request the use of biological resources which belong to biobanks which are part of National nodes networks of BBMRI-ERIC member countries? *Biological resources means biological samples and/or associated data, including genetic data.*	□	□	Austria □ Belgium □ Czech Republic □ Estonia □ Finland □ France □ Germany □ Greece □ Italy □ Malta □ Norway □ The Netherlands □ Sweden □ UK □ Do not know yet *(please justify)* □
Does this research request the / already use biological resources which belong to biobanks established in other EU countries? *Including non-BBMRI-ERIC countries and BBMRI-ERIC observer countries*	□	□	*Please specify the countries, the resources and the page[4] describing the modalities for their use*
Does this research request the / already use biological resources which belong to biobanks established in non-EU countries?	□	□	

[4] References shall be done to the page numbers of relevant sections in the scientific documents provided that describe the project. Examples: for a block of consecutive pages, ex: p.45-48. For separated pages, ex: p.12; 17.

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Including non-BBMRI-ERIC countries and BBMRI-ERIC observer countries				
If YES	Is it planned to import biological resources – including personal data – from non-EU countries into the EU?	☐	☐	*Please specify the countries, the resources and the page[1] describing the modalities for their use*
	Is it planned to export biological resources – including personal data –from the EU to non-EU countries?	☐	☐	*Please specify the countries, the resources and the page[1] describing the modalities for their use*
	Is it planned to use local resources (e.g. human remains or materials of historical value, traditional knowledge etc.)?	☐	☐	*Please specify the countries, the resources and the page[1] describing the modalities for their use*
	In case this research involves low and/or lower-middle income countries, are any benefit-sharing actions planned?	☐	☐	*Page[1]*
Item 3: RESEARCH CENTRES INVOLVED		YES/NO		Tick as appropriate
Will the resources be managed (e.g. stored) in centres that are part of BBMRI-ERIC National nodes networks? *Including non-BBMRI-ERIC countries and BBMRI-ERIC observer countries*		☐	☐	Austria ☐ Belgium ☐ Czech Republic ☐ Estonia ☐ Finland ☐ France ☐ Germany ☐ Greece ☐ Italy ☐ Malta ☐ Norway ☐ The Netherlands ☐ Sweden ☐ UK ☐ Do not know yet *(please*

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				justify) □
If **NO or if other countries are also involved :**	Will the resources be managed in centres located in other EU countries?	□	□	*Please specify the countries and page*[1]
	Will the resources be managed in centres located in non-EU countries?	□	□	*Please specify the countries and page*[1]

Item 4: HUMAN SAMPLES AND DATA SOURCES	YES/NO		Page
Does this research relates to the following categories of persons as original sources of the samples/data to be used?			
- Healthy volunteers?	□	□	*Please indicate the page*[1] *where selection criteria and modalities for respecting individuals' rights are described*
- Persons unable to give informed consent?	□	□	*Please indicate the page*[1] *where selection criteria and modalities for respecting individuals' rights are described*
- Vulnerable individuals or groups?	□	□	*Please indicate the page*[1] *where selection criteria and modalities for respecting individuals' rights are described*
- Children/minors?	□	□	*Please indicate the page*[1] *where selection criteria and modalities for respecting individuals' rights are described*
- Patients?	□	□	*Please indicate the page*[1] *where selection criteria and modalities for respecting individuals' rights are described*
- Existing database?	□	□	*Please indicate the page*[1] *where selection criteria and modalities for the access and respect of individuals' rights are*

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				described
Item 5: HUMAN CELLS / TISSUES		YES/NO		Page [1]
Does this research involve the use of human tissues / cells which are part of BBMRI-ERIC? (*other than from Human Embryos/Foetuses, see below)*		☐	☐	
If **YES:**	- Please, specify the type and quantity of tissues / cells			Type(s): Quantity[5]:
If **NO**:	- Are they available commercially?	☐	☐	
	- Are they obtained from another project, laboratory or institution?	☐	☐	
	- Are they intended to be used for developing biotechnologies or commercial products within this project?	☐	☐	
	- Please, specify the type and quantity of tissues / cells			Type(s): Quantity[2]:
Does this research involve Human Embryonic Stem Cells (hESCs)?		☐	☐	
If **YES**:	- Are they accessed through BBMRI-ERIC?	☐	☐	
	- Will they be directly derived from human embryos within this project?	☐	☐	
	- Are they derived from previously established cells lines?	☐	☐	
	- Please, specify the type and quantity of stem cells			Type(s): Quantity[2]:
Does this research involve the use of human embryos?		☐	☐	
If **YES:**	- Are they accessed through BBMRI-ERIC?	☐	☐	
	- Please, specify the quantity of requested/involved stem cells			
Does this research involve the use of human foetal tissues/cells?		☐	☐	
If **YES:**	- Are they accessed through BBMRI-ERIC?	☐	☐	
	- Please, specify the type and quantity of requested/involved stem cells			

[5] Sample size and/or quantity of each sample as relevant.

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Does this research involve the setting up of a new biobank?		☐	☐	
Item 6: MICRO-ORGANISMS		YES/NO		Page [1]
Does this research involve the use of micro-organisms of human origin?		☐	☐	
Does this research involve the use of genetically modified organisms of human origin?		☐	☐	
Does this research involve the use of pathogenic micro-organisms of human origin?		☐	☐	
Item 7: PERSONAL DATA		YES/NO		Page [1]
Does this research involve personal data collection and/or processing?		☐	☐	
If **YES**:	- Does it involve the collection and/or processing of sensitive personal data *(e.g. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)*?	☐	☐	
	- Does it involve processing of genetic information?	☐	☐	
	- Does it involve tracking or observation of participants?	☐	☐	
	- Is it likely that the study will produce (personal) health related information that could be important for an individual participant to know, like strong possibility of disease with known cure?	☐	☐	
Does this research involve BBMRI-IT platforms or services?		☐	☐	
Does this research involve the setting up of a new database?		☐	☐	
Item 8: ENVIRONMENT & HEALTH AND SAFETY		YES/NO		Page [1]
Does this research involve the use of elements that may cause harm to the environment, to animals or plants?		☐	☐	
Does this research involve the use of elements that may cause harm to humans, including research staff?		☐	☐	
Item 9: DUAL USE		YES/NO		Page [1]

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Does this research have the potential for military applications?	☐	☐	
Item 10: MISUSE	YES/NO		Page [1]
Does this research have the potential for malevolent/criminal/terrorist abuse?	☐	☐	
Item 11: OTHER ETHICS ISSUES	YES/NO		Page [1]
Are there any other ethics issues that should be taken into consideration? If **YES**: *please specify*	☐	☐	

STEP 2: Ethics Check by the BBMRI-ERIC Common Service ELSI (Procedure B only)

The step 2 intends to check the information provided by the applicant with regard to the self-assessment table used for step 1 (above).
In step 2, CS ELSI experts are requested to provide an opinion regarding the project and its modalities with due regard to the requirements of enforceable legal framework, ethical principles, guidelines and best practices, as described in the Ethics Check Operational Procedure (available on the intranet).

- **Legal / ethical benchmark of the checking:**
  The following criteria have to be scrutinized with regard to the relevant European or international laws and regulations including relevant ethical guidelines and opinions.

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This includes, in particular, the following instruments:

Binding instruments:

- European Convention for the Protection of Human Rights and Fundamental Freedoms, 1950;
- Charter of Fundamental Rights of the European Union, OJC 326, 26 October 2012.
- Council of Europe Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (Oviedo Convention), 4 April 1997; as well as relevant additional protocols such as Additional Protocol on the Prohibition of Cloning Human Beings, 12 January 1998;
- Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells;
- Directive 2006/17/EC implementing Directive 2004/23/EC as regards certain technical requirements for the donation, procurement and testing of human tissues and cells;
- Directive 2006/86/EC implementing Directive 2004/23/EC as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells;
- Directive 98/44/EC **of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions;**
- Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data (to be replaced by the EU General Data Protection Regulation as soon as it will be adopted and in force);
- Directive 2002/58/EC of the European Parliament and of the Council of 12 July 2002 concerning the processing of personal data and the protection of privacy in the electronic communications sector.

Non-binding instruments:

- WMA Declaration of Helsinki, Brazil, 2013;
- OCDE Guidelines for Human Biobanks and Genetic Research Databases (HBGRDs), 2009;

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- Council of Europe Rec(2004)10 concerning the Protection of the Human Rights and Dignity of Persons with Mental Disorder;
- Council of Europe Rec(2006)4 on Research on Biological Materials of Human Origin
- ISBER Best practices for repositories: collection, storage, retrieval, and distribution of biological materials for research, third edition, 2012;
- EGE, European Group on Ethics in Science and New Technologies relevant Opinions
- Article 29 Data Protection Working Party opinions and recommendations
- EuroBioBank SOPs
- OECD Principles and Guidelines for Access to Research Data from Public Funding, 2007.
- Global alliance, International code of conduct for genomic and health-related data sharing;
- HUGO Ethics Committee Statement on benefit sharing, 2009.
- Singapore Statement on Research Integrity, 2010.

Other instruments can be used as a basis of the Ethics Check, notably the BBMRI-ERIC policies, where it is relevant in the context of a specific project.

- **Checking criteria** (and related item from step 1, see the self-assessment table above)
  Note: The below-defined criteria are conceived as guiding elements for experts involved in the checking. Where relevant, other legitimate elements can be taken into account regarding a specific research.

N°	Criteria to check	Relevant item(s) from step 1
1	Explanation about the scientific goals of the activities planned and explanation on the benefits of the research for individuals/society. This shall be checked regarding the research protocol.	**Item 1**
2	Clear information about the European scheme of the research (partners and countries, flow chart stating the geographical sources and destinations of samples, partners' tasks regarding samples and data to be used).	**Items 2,3, 9**
3	Justification of the necessity to use biological samples regarding the research purposes (risk/benefit assessment).	**Items 4, 5, 6**
4	Justification of the necessity to use personal data regarding the research purposes – (risk/benefit	

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	assessment).	**Item 7**
5	Details on the types of resources, number, quantity, context and authorisation(s) obtained by the primary owner (including references to ethics approval obtained or applied for).	**Items 5, 6, 7**
6	Details about the procedure(s) ensuring the respect of informed consent / agreement from research participants (e.g. voluntariness and no financial gain shall be ensured; confirmation that informed consent and/or appropriate approval has been obtained and covers the reuses, including the international sharing, import/export, of samples and/or data for the needs of the project; potential further envisaged retention or uses after the project).	**Items 2, 3, 4, 5, 7, 11**
7	Details on the management of the samples collections and databases including information regarding responsible institutions, custodian(s) and users of the resources in relation with a research task (e.g. kind of activity performed and purpose(s), duration of storage, security, quality and accountability principles, professionals identity and appropriate background/training, details about what will be done with the resources at the end of the research. Any agreements or contracts allowing to access and use these sources should also be included. It is also recommended to check if a cost/benefit assessment is performed specifically where a new biobank/database will be set up).	**All ticked items**
8	Details on the policy and procedures for the access and use of the collections of samples/data in compliance with EU laws and, where relevant, measures regarding participants' rights compliance and exercise.	**All ticket items**
9	Details about the privacy policy, data protection and the management of incidental findings (In particular where genetic data are used or generated).	**Items 5, 7**
10	Security and safety measures regarding micro-organisms or GMOs; authorisations, quality and security controls, sites' description and suitability for carrying out proposed research and minimize identified risks.	**Items 2, 3, 7, 9**
11	Details on activities carried out in non-EU countries including explicit confirmation that the activities could have been legally carried out in an EU Member States.	

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	Clear flow chart(s); appropriate safeguards and terms of uses; contracts**.** Check of the existence of any Convention to respect or of European Commission decisions regarding adequacy of data protection level.	**Item 2, 3**
12	Risk/benefit analysis including details on the measures planned to mitigate identified risks (E.g. regarding personal data this exercise can take the form of a data protection impact assessment).	**All ticked items**
13	Adequacy of ethical (e.g. guidelines) and legal documents (e.g. laws) referred regarding the envisaged activities.	**All ticked items**
14	ELSI management along the project (E.g. ELSI internal management board/expert).	**All ticked items**
15	Confirmation that the ethical and legal international or European texts referred through the project will be rigorously applied, regardless of the country in which the research activities are carried out.	**All ticked items**
16	Existence and relevance of the documentation provided in support of the project/program regarding the issues at stake (informed consent form and information notice; copies of relevant ethics approvals, authorisations from competent authorities, certifications, MTA etc.)	**All ticked items**

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BBMRI-ERIC COMMON SERVICE ELSI ETHICS CHECK – OPERATIONAL PROCEDURE (DRAFT)

Object of the document

This document describes the internal rules regarding:

- The submission of the projects/programs submitted to the Ethics Check procedure and accepted according to the Ethics Check Criteria defined in the eponym document, and
- The participation of experts involved in the Common Service ELSI (here after CS ELSI) Ethics Check,
- The formulation of experts' opinions.

The Ethics Check consists in an analysis of the ethical, legal and social implications of research projects or programmes in accordance with a specified list of considerations established in the document "Ethics Check Criteria".
The Ethics Check is intended to provide an opinion to the BBMRI-ERIC headquarters and recommendations to research promoters or investigators regarding the ethical legal and social implications (ELSI) arising from their research project/programme.
Recommendations can also be given regarding further investigations of ELSI issues that should be carried out within a specific project/programme.

Procedure

4- Submission of a research project/programme subject to an Ethics Check

Any research promoter whose project/programme is responding to the submission criteria described in the document "Ethics Check Criteria" must apply for an Ethics Check to BBMRI-ERIC.
Note: When an ethics review has been done or will be done within the Horizon 2020 Programme there will be no Ethics Check performed by the BBMRI-ERIC. However, in such cases, the CS ELSI can be asked for advice in the preparation of the ethics part, in order to meet the European Commission requirements or answer to recommendations.
Applications for a Common Service ELSI Ethics Check can be done through:

- an online request using the BBMRI-ERIC website (one stop-shop[6])
- a written request from the Director of BBMRI-ERIC.

[6] The tool for submitting projects for the CS ELSI Ethics check is presently under construction.

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- a written request from a research promoter/principal investigator of a BBMRI-ERIC member State
- a written request from a research promoter/principal investigator of a BBMRI - ERIC Observer State
- a request from another ERIC, as a transversal support.

Any application is followed by an acknowledgement.
Any application and related documentation will be communicated to the secretary of the BBMRI-ERIC CS ELSI. The secretary will organize the Ethics Check in collaboration with the Coordinator of the CS ELSI, e.g. contact of the experts involved etc.

5- Selection of experts for the purpose of the Ethics Check

Experts involved for performing the interdisciplinary Ethics Check are selected with the help of an internal BBMRI-ERIC CS ELSI Experts' database (*presently in construction*) including both European and international recognized professionals skilled in relevant domains, notably in life sciences, law, ethics, social sciences, medicine and technology. 2-4 experts are selected per project/program depending on the number of countries involved; 1 expert is appointed as rapporteur. The selection process is further described below.

Selection process:

- The number of experts to mobilise for a project/program is established at the CS ELSI Coordination level at the time of the reception of the ethics table and related documents. This is done according to the apparent characteristics or complexity of the application (e.g. number of identified ELSI issues; length of the documents; number of partners to the project/program).
- A first pool of qualified persons is constituted using the ELSI Experts' database *(under construction),* in the respect of non-discrimination principle.
    - Experts are targeted according to the field(s) of the research to be checked;
    - Where specific skills (e.g. linguistic skills) are necessary for the purpose of the Ethics Check, it will be possible to use specific criteria for the randomised selection (e.g. nationality). This could be done either for setting up the original pool of experts, or under request from the selected experts involved in the Ethics Check.
- From this pool, 2-4 experts are selected randomly.
- The CS ELSI Secretary contacts each of the selected experts and ask for their consent to participate to the Ethics Check. Experts are free to refuse participation.
- Upon receiving consent from each expert confirming their availability, the CS ELSI Secretary send the necessary documents to perform the Ethics Check,

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inform about the deadline for providing the opinion and ask for a designation of the rapporteur.

6- General rules for participating as an expert in the Ethics Check

a. All the experts involved must respect professional secrecy and confidentiality in the processing of the projects/programmes submitted to the Ethics Checking procedure.
b. The presence of a conflict of interest is incompatible with the exercise of the Ethics Check. Each ELSI expert shall sign an individual declaration stating that she/he has no interest link[7] that could influence the opinion on a project/programme to be checked.
c. Experts should be appointed based on their expertise in ELSI and acquaintance with national/local regulations and language.
d. A rapporteur ensures the drafting of the opinion and recommendations and its appropriate communication to the experts involved for approval. The rapporteur then reports the opinion and recommendations to the research investigator and to the CS ELSI secretary for recording and sending to the BBMRI-ERIC headquarter.

7- Delay in processing applications:

The entire Ethics Check procedure must not take longer than **4 weeks**.

This delay of 4 weeks to achieve the Ethics Check starts to run from the date of the reception of the complete application. At this time, the applicant is informed about the applicable timeline.

Where a supplementary delay is necessary, the applicant shall be informed. The 4 weeks delay can only be repeated once.

In case of impossibility to implement the Ethics Check in an 8 weeks delay, the opinion is deemed as positive. The burden of proof regarding the exceeding of announced deadlines relies on the applicant.

8- Standard formulation of the opinion:

[7] Persons who do not have conflicts of interest, are independent from the promoter/sponsor, research centers involved, investigators involved and persons financing the research, as well as free of any other undue influence such as financial or personal interests which could affect impartiality. In case of conflict, the person shall not participate in the ethics check.

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The opinion of the experts is given with comments on the specific considerations laid out in the Ethics Check list. It is concluded with alternatives as follows:

- Recommended to accept
- Admissible under specific modifications (with recommendations)
- Recommended not to accept (with mandatory motivation and recommendations)
- Recommended for further investigations of ELSI issues within the project/programme (with recommendations; investigations to be done by the promoter/principal investigator).

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