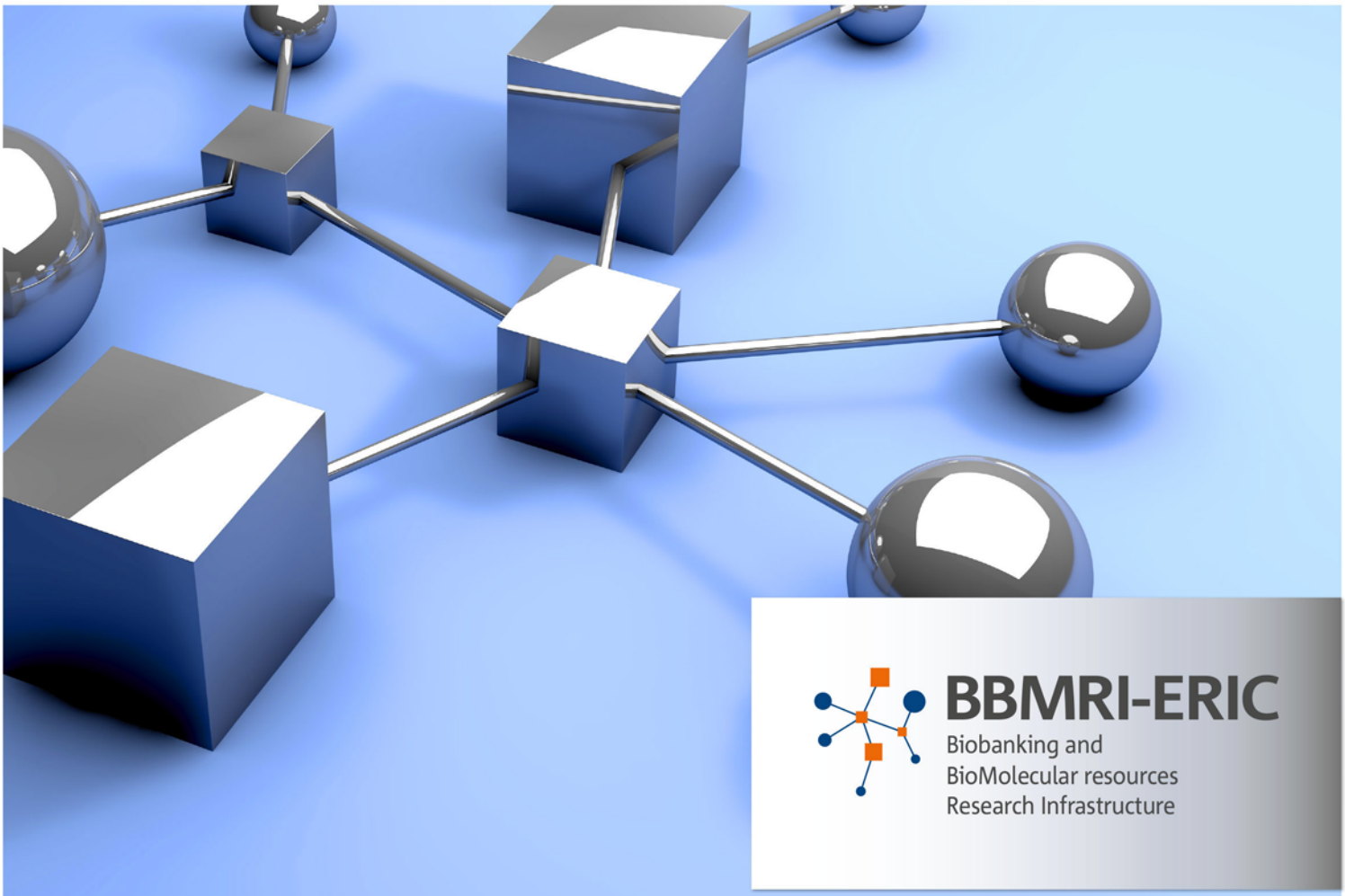

BBMRI-ERIC
Biobanking and
BioMolecular resources
Research Infrastructure

Comments to the public consultation on the Council of Europe Recommendation (2006)4 on research on biological materials of human origin

2014/08/14

Important information

This participation to the public consultation on the Council of Europe Recommendation (2006)4 on research on biological materials of human origin is performed on behalf of BBMRI-ERIC after internal consultation of experts on ethical legal and social issues.

BBMRI-ERIC – officially awarded the Community legal framework for a European Research Infrastructure Consortium on 3 December 2013, shall establish, operate and develop a pan-European distributed research infrastructure of biobanks and biomolecular resources in order to facilitate the access to resources as well as facilities and to support high quality biomolecular and medical research. BBMRI-ERIC operates on a non-economic basis.

As of today, BBMRI-ERIC consists of 16 Member States and one International Organisation, making it one of the largest research infrastructures for health research in Europe.

Members: Austria, Belgium, Czech Republic, Estonia, Finland, France, Germany, Greece, Italy, Malta, the Netherlands, Sweden
Observer Countries/International organisation: Norway, Poland, Switzerland, Turkey, IARC/WHO

Therefore, the comments exposed below represent a joint contribution from BBMRI-ERIC National Nodes set up in the Member Countries and do not represent any governmental position. The experts involved worked independently.

Comments are provided article by article. General comments are also formulated.
Where discrepancies emerged from this collaborative work they are reported accordingly. For these only, the National Node is explicitly mentioned as the source.

While we deeply acknowledge the revision works undertaken by the Council of Europe on this major text, we hope that this European contribution will be valuable for advancing this updating.

The blue color is used to highlight the propositional aspects of the comments.

COUNCIL OF EUROPE

COMMITTEE OF MINISTERS

Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin

(Working document version – 18th of March 2014)

Preamble

The Committee of Ministers, under the terms of Article 15.*b* of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is the achievement of greater unity between its members and that one of the methods by which this aim is pursued is the maintenance and further realisation of human rights and fundamental freedoms;

Considering that one of the aims of the Convention for the Protection of Human Rights and Fundamental Freedoms (ETS No. 5) is the protection of private life;

Considering that the aim of the Convention on Human Rights and Biomedicine (ETS No. 164, hereinafter referred to as "the Convention") and of its Additional Protocol concerning biomedical research (CETS No. 195), as defined in Article 1 of both instruments, is to protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine;

Considering that progress in medical and biological sciences, in particular advances obtained through biomedical research, including research using biological materials donated in a spirit of solidarity**,** contributes to saving lives and improving their quality;

Conscious of the fact that the advancement of biomedical science and practice is dependent on knowledge and discovery which necessitates research on human beings and research involving the use of biological materials of human origin;

Stressing that such research is often transdisciplinary and international;

Taking into account the current and planned development of collections of biological materials at national level;

Stressing the importance of the right to privacy in the field of biomedical research, as defined in data protection instruments;

Taking into account the development of new technologies, in particular in the field of genetics, which increase issues regarding privacy and feedback on incidental health-related findings;

Taking into account the establishment of international research infrastructures that pool and share samples and data across national borders;

Taking into account national and international professional standards in the area of biomedical research and the previous work of the Committee of Ministers and the Parliamentary Assembly of the Council of Europe in this field;

Stressing that the paramount concern should be the protection of the human being whose biological materials are obtained, stored or used for research;

Recalling that research on biological materials should be carried out freely subject to the provisions of this Recommendation and the other legal provisions ensuring the protection of the human being;

Emphasising that the interests and welfare of the human being whose biological materials are used in research shall prevail over the sole interest of society or science;

Affirming that particular protection shall be given to human beings who may be vulnerable in the context of research, especially to those who are not able to consent;

Recognising that every person has the right to accept or refuse to contribute to biomedical research and that no one should be forced to contribute to it;

Stressing the importance of good and transparent governance of biological materials stored for research purposes;

Stressing that collections developed on the basis of donations of biological materials made in a spirit of solidarity should not be monopolised by small groups of researchers;

Recognising the value for biomedical research of existing collections set up for clinical purposes;

Resolving to take such measures as are necessary to safeguard human dignity and the rights and fundamental freedoms of the individual with regard to biomedical research on biological materials of human origin,

Recommends the governments of member states:

a. to adapt their laws and practices to ensure the implementation, including its follow-up, of the guidelines contained in the appendix to this Recommendation, which replaces Rec(2006)4;

b. to promote the establishment of codes of good practice to ensure compliance with the guidelines contained in this appendix;

Entrust the Secretary General of the Council of Europe to transmit this Recommendation to the governments of the non-member states of the Council of Europe, which have been invited to sign the Convention on Human Rights and Biomedicine, to the European Union and to other relevant governmental and non-governmental international organisations.
* * *

Appendix to Recommendation Rec(2006)4

Comments about Recitals (where relevant, cite the text)

The preamble is not very balanced. There are many provisions and repetitions regarding privacy, protection of human etc. but only one provision regarding interests of medical and biomedical science and benefits. One should remember that freedom of research and right to pursue professional activities are also fundamental rights. In addition, this kind of an approach seems to reflect traditional regulation on clinical trials on humans, but biobanks only collect biological specimens and research only use samples in repositories. *Which welfare issues are really at stake?*

Guidelines

GENERAL COMMENTS ON THE WHOLE TEXT

Proposal for textual harmonisation:
Why not using the terms « human biological resources » as the pooling of human biological samples and associated (personal) data, according to the work done by the OECD on this matter? Also the term "samples" is preferred to "materials" and we recommend using the term "biobank" as it has been defined or inspiring from the definition provided in the EU Commission Implementing Decision (2013/701/EU) fixing the status of BBMRI-ERIC (http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:320:0063:0080:EN:PDF): "Biobanks (and Biomolecular Resources Centres)' means collections, repositories and distribution centres of all types of human biological samples, such as blood, tissues, cells or DNA and/or related data such as associated clinical and research data, as well as biomolecular resources, including model- and micro-organisms that might contribute to the understanding of the physiology and diseases of humans".
This would give more consistency to the European framework and would allow clarifying the scope and the rules that would become thus much more operational.

Comment about the content:
Overall there is significant room for national interpretation and while many of the subjects could be clearer – and we would like them to be clearer - it is not certain that consensus could ever be reached, at least not without ending up with recommendations which are the most restrictive and complicated. Best to leave it flexible and let member states write their own laws or regulatory texts.
This commendable proposal to guarantee the patient's rights does however not take into account existing mechanisms with the same purpose. E.g. in several countries like Belgium, France, ethical committees, established by law, control the creation of biobanks, the storage of samples and their use in any study. It would be wise to leave enough room for those existing mechanisms to be kept and strengthened and look into these existing mechanisms for inspiration. These guidelines should therefore give a general framework that can be implemented on the national level using the mechanisms that are already in place.

The focus of the draft is not just about research, but also about collecting and storing samples for the purposes of future research, whose exact nature is not necessarily known at the time of collection/storage. The role of biobanks and the role of researchers in a specific project are different, and each provision should be checked against this background. Thus, biobank governance and use for research/approval of research plans are different.

The recommendation should reflect rights to privacy as well as rights of access to preventive health care and the right to benefit from medical treatment:
The preamble rightly states the significance of protecting private life. However it should also explicitly address the rights of each citizen to prevention and medical treatment. In agreement with the European Convention for the Protection of Human Rights and Fundamental Freedoms, the Social Charters adopted by the Union and by the Council of Europe, the Charter of Fundamental Rights of the European Union (2010/C 83/02) emphasizes the right of each individual to integrity within the fields of medicine and biology, implying a free and informed consent according to the procedures laid down by law (Article 3). Article 8 grants the individual the right to the protection of personal data concerning him or her, implying that processing of such data requires consent of the person concerned or some other legitimate basis laid down by law. These and other rights in the charter may be motivated by a fundamental respect of each individual's autonomy and right to have control of matters related to oneself, e.g. the processing of personal data and the use of biological samples of human origin. In addition to these autonomy rights the Charter of Fundamental Rights of the European Union also lays down rights of each individual to social security benefits and social services in cases of illness (Article 34) and the rights of access to preventive health care and the right to benefit from medical treatment under the conditions established by national laws and practices (Article 35). As described, the charter of the European Union recognizes both the autonomy right and the right to health care and social services in cases of illness as fundamental individual rights, notwithstanding that there may also be societal and public health related interests concerned.

The development of a quality health care and the safeguarding of a high level of excellence in health care depends on the persistence of biomedical research also based on residual material. This aspect must be highlighted in communications to the public and legislation. So the patient can understand the importance of his/her contribution occurring in a legal and ethical framework for the use of biological samples and associated

data. Also, samples and data have been entrusted to the researcher/biobank/institution. Thereof, their responsibility to use the samples for the development of medicines and better healthcare could be deduced.

Regarding privacy:
Does the use of anonymised samples safeguard human dignity? Why build up a strict procedure for collection and use of identifiable samples, but keep it light/non-existent when anonymised? Is the recommendation mostly about data protection? Then it is unnecessary, as we have already very strict data protection regimes at European level, and reference to EU and CoE such texts could be made explicitly. We however acknowledge that such a recommendation can be used in other countries than the European ones.

Proposal for a clear table/chapter of key terms definitions:
Some of the terms used may be read/"interpreted" in different manner (i.e. human sample resource, anonymised, coded etc) and, since this is a recommendation could be taken into consideration also from other than European geographic areas, where "wording use" may be quite different, we suggest to add a very short table / chapter with the definition of main terms used in the document. We know that no absolute definitions exist but it is good practice in legislation on European and international level to introduce some key terms by such a table of definitions ("For the purposes of this recommendation…").
Specific/contextual comments about this crucial issue can be found throughout this contribution.
This table should be aligned with existing documents in Europe, e.g. the Oviedo Convention and relevant protocols, EU legislation such as the Directive 95/46/EC, and at least include the following terms:

- "pseudonymised" (instead of "coded"),
- "biological material" or other chosen term (see supra proposals about human biological resources and the term "samples")
- "collection of biological material" or other chosen term (see supra proposals about "biobank"),
- "removal of biological material",
- "family",
- "same group of individuals",
- "persons concerned",
- "consent" (freely given)
- "authorisation".

CHAPTER I **Object, scope and definitions** **Article 1 – Object** Member states should protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity, right to private life and other rights and fundamental freedoms with regard to any research governed by this recommendation.	"Member states should protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity, right to private life and other rights and fundamental freedoms with regard to any research involving their biological samples governed by this recommendation."
Article 2 – Scope 1. This Recommendation applies to - the obtaining of biological materials of human origin for storage for future research purposes; - the storage of biological materials of human origin for future research purposes; and - the use in a research project of biological materials of human origin that are stored or were previously obtained for another purpose, including a previous research project.	**Para. 1.** **Proposal of specifications:** Does this Recommendation apply to microorganisms of human origin? To what extent? Proposal: Insert an explicit referral to the obtaining, the storage, the use of microbial materials contained in human biological samples (or human clinical isolates) Are the blood, urine, hairs included? Does a specific procurement of human biological sample for future research purposes is in the scope of this Recommendation? In such a case, is this covered by paragraph

2. This Recommendation does not apply to - embryonic and foetal tissues; and - the use in a specific research project of biological materials of human origin removed for that purpose. This is within the scope of the Additional Protocol concerning Biomedical Research (CETS No. 195). 3. The collection, storage and use of biological materials of human origin may be accompanied by associated personal data. Where in this Recommendation provisions make reference to biological materials of human origin these extend, where relevant, also to associated personal data.	2 and thus only by the Additional protocol CETS No.195? Need for clarifications about the articulation between these texts. From this article, the position of the actual recommendation on biomaterial collected for primary diagnostic use and/or surgical left over is not clear. Left materials after diagnosis and/or surgical and/or clinical trials may be destined to future research only if there is a warranty of quality management of the material from the collection. Under the right circumstances this "residual biological material" is a valuable source of human biological resources for research that would otherwise be destroyed. A direct mention of this material should be included in this section. Also it is proposed to refer to "residual biological material/samples". **Para. 2.** - the obtaining, storage and use in a specific research project of biological materials of human origin removed for the sole purpose of that project. This is within the scope of the Additional Protocol concerning Biomedical Research (CETS No. 195). **Para. 3.** **Proposal of specifications:** …these extend, where relevant according to Article 3, also to associated personal data (link with the Council of Europe Convention N°108, http://conventions.coe.int/Treaty/en/Treaties/Html/108.htm) …
Article 3 – Identifiability of biological materials Biological materials referred to in Article 2 may be identifiable or non-identifiable: i. *Identifiable biological materials* are those biological materials which, alone or in combination with data, allow the identification of the persons from whom the materials have been removed, either directly or through the use of a code. In the latter case, hereafter referred to as "coded materials", the user of the biological materials may have direct access to the code or, alternatively the code may be under the control of a third party. ii. *Non-identifiable biological materials*, hereafter referred to as "anonymised materials", are those biological materials which, alone or in combination with data, do not allow, with reasonable efforts, the identification of the persons from whom the materials have been removed.	**General comment on Chapter 1:** It would be necessary to define the terms "biological materials" (or "human biological resources" or "identifiable/non-identifiable human biological samples" as suggested earlier) as well as the term "collection", used in the recommendations (e.g. Chapter V) within this Chapter or in a separated section of Definitions; Also, for this latter we propose to change the term "collection" by the new commonly used "biobank" term or to explain the difference between these two terms.. **Comment on "Anonymised"** The given definition of "anonymised materials" is questionable and subject to an ongoing debate in the scientific community, as the (genetic) information within the material itself in principle allows an identification of the person from whom the materials have been removed. Subject to anonymisation can only be the meta data coming along with the material. The material as such contains the full genome. As sequencing has become quite feasible and affordable, the concept of anonymising biological material is challenged to an extent that it should not be used without a clear statement of the risk.

CHAPTER II **General provisions** **Article 4 – Risks and benefits** 1. The risks for the persons from whom biological materials have been removed and, where appropriate, for their family, related to research activities, in particular the risks to private life, should be minimised, taking into account the nature of the research activity. Furthermore, those risks should not be disproportionate to the potential benefit of the research activities. 2. Possible risks for the individuals in the same group as the person from whom biological materials have been removed should also be taken into consideration in this context.	**Para. 1.** **Proposal for textual specifications** Specify the notion of "family" and/or refer to national laws. **Proposal of textual modification** The risks for the persons from whom biological materials have been removed and, where appropriate, for their family or their relatives, related to research activities, in particular the risks to private life, should be minimised, taking into account the nature of the research activity. **Para. 2.** **Proposal of modification** Possible risks or benefits for the individuals in the same group as the person from whom biological materials have been removed should also be taken into consideration in this context. **Proposal of textual specifications** Specify who are the "individuals in the same group". It would be appropriate to give some examples, in order to avoid misunderstanding and facilitate the application of this paragraph.
Article 5 – Non-discrimination 1. Appropriate measures should be taken, in the full range of research activities, to avoid discrimination against, or stigmatisation of, a person, family or group. 2. Refusal to give consent or authorisation to the removal, storage or research use of biological materials or the withdrawal or alteration of the scope of the consent or authorisation given should not lead to any form of discrimination against the person from whom biological materials have been removed, in particular regarding the right to medical care.	**Para. 2.** **Proposal of textual clarification:** "Refusal to give consent or authorisation…" What does the term "authorisation" mean in the context of this text, what is the difference with the consent notion as used along this Recommendation? Does it refer to consent given on behalf of a person by somebody else (a competent representative or authority, when so provided by law)? Such key terms should be clearly and consensually defined in order to enhance harmonisation while keeping the possibility to refer to national laws for specific detailed definitions). Clarification is needed: authorisation vs informed consent vs opting-out or presumed consent.
Article 6 – Prohibition of financial gain Biological materials should not, as such, give rise to financial gain.	**Proposals of adds** Biological materials should not, as such, give rise to financial gain or patrimonial provisions. ***Proposed add:*** …"without prejudice to intellectual property rights or legitimate rewarding provided by law". E.g. fees for maintaining the quality of the biological resources.

	Proposed add: "Production costs if the material has been transformed, characterized, purified, produced can nonetheless be charged".
Article 7 – Justification of identifiability 1. Biological materials should be anonymised as far as appropriate to the research activities concerned. 2. Any use of biological materials in an identifiable form should be justified in advance by the researcher.	**Proposal to insert a new paragraph about the principle (e.g. new para. 1):** E.g. "Use of directly identified human biological resources should be an exception. Human biological resources should be pseudonymised as far as appropriate to the research activities concerned". **Related comments on "anonymisation":** Perhaps it should be clarified, that the collection does not need to be anonymised - i.e. a biobank can (probably should) be able to identify the material/resource (through a code etc.) but for individual research purposes the material would be coded/pseudonymised again? The concept of anonymising human biological material/resources as a means to enable research without explicit consent is not in conformity with standards in data security (e.g. in Germany). "Anonymisation" of biological material/resource does not only restrain research, (no possibility of adding and updating of supplementary information) but also restrains the donor in its right to object to any further research on a given probe. Thus it is preferred to destroy donated biological materials/resources upon consent withdrawal. However, if for certain research purposes human biological materials/resources maintained and anonymised are appropriate, it is mandatory to inform the donor on the risk that withdrawal of consent for biomedical use of the donated material/resource and/or its destruction is no more possible. In contrast, anonymisation of the meta data (not the materials/samples as such - see above) is feasible but is not generally recommended, since it always retails the right of withdrawal. In addition, feeding back any incidental findings is no more feasible. Therefore pseudonymisation is generally preferred. **Proposal of add about the characterisation of identifiability:** Where the researcher or another person handling the materials/human biological resources does not have a need to identify the persons from whom the materials have been removed, and where such identification is disabled by sufficient technical and other means, the materials/human biological resources may be considered as non-identifiable human biological materials/human biological resources for the purposes of handling by such a party.
Article 8 – Confidentiality 1. Any information of a personal nature collected at the time of removal, storage or use of biological materials, or obtained through research should be considered as confidential	

and treated according to the rules relating to the protection of private life. 2. Appropriate security measures should be in place to ensure confidentiality at the time of removal, storage, use and, where appropriate, transfer of biological materials.	
Article 9 – Public information Member States should take appropriate measures to facilitate access for the public to general information on the nature and objective of research collections and on the conditions relating to the obtaining, storage and use of biological materials for research purposes, including matters relating to consent or authorisation.	
Article 10 – Wider protection None of the provisions of this Recommendation should be interpreted as limiting or otherwise affecting the possibility for a member state to grant a wider measure of protection than is stipulated in this Recommendation.	
CHAPTER III – Information and consent	**General comment:** **Information and consent procedures needs elaboration:** There is accordingly a need of balancing autonomy rights and rights to health care, prevention and medical treatment, and this needs to be better described in the guidelines. The present formulation of Chapter III, Article 11 does not reflect the rights of access to preventive health care and the right to benefit from medical treatment to be acquired with the help of biomedical research.
Article 11 – Removal of biological materials for storage for future research ***Information*** 1. Prior to requesting consent to remove biological materials for storage for future research, the person concerned should be provided with comprehensible information: i. that is specific with regard to the intervention carried out to remove the materials; and ii. that is as precise as possible with regard to: - any research use foreseen; - the conditions applicable to the storage of the materials; and - other relevant conditions governing the	**General comment:** It has to be notified that this article 11 does not apply to "residual biological material" as defined e.g. in the Belgian law. Proposal: either modification of the title replaced by "Removal of biological materials exclusively for storage for future research" and additional article on "residual biological material" (i.e. presumed consent) or extension of article. (cf. art 13) **Inconsistency** Having regard to the elected scope of the recommendation, i.e. that the recommendation applies only to the obtaining and storage of biological materials of human origin for storage for future research purposes and the use of biospecimens previously obtained for another purpose (Art.2) the requirements in Art 11 that information and consent should

use of the materials. 2. The persons concerned should also be informed of the rights and safeguards prescribed by law for their protection. 3. The persons concerned should be offered the possibility to exercise choices with regard to the type of research use of their biological materials. ***Consent*** 4. Biological materials may not be removed for storage for future research without the free, express and documented consent of the person concerned: - that is specific with regard to the intervention carried out to remove the materials; and - that is as precise as possible with regard to the research use covered, in the light of the information provided in paragraph 1, ii., and includes possible choices made in accordance with paragraph 3.	be specific about the intervention carried out to remove the materials is, at best, misleading since it doesn't apply to already collected materials. **General comment/Question:** Does the practice of a broad consent is respecting this provision? **Related proposal for modifications (to the above comment/question) :** The recommendation that information and consent should be as precise as possible with regard to the research use is also potentially misleading since the sampling referred to is for future research with only general purposes described. It is today also common knowledge within biobank based research that samples collected for general medical purposes, e.g. for research on cardiovascular diseases, often later tusks out to deliver great benefit for patients with other types of diseases, e.g. identification of early factors behind Rheumatoid Arthritis 10-15 years before onset through a cardiovascular biobank. Research like this is of tremendous importance for early detection and treatment of Rheumatoid Arthiritis (ref. Eriksson C, et al, Arthritis Res Ther. 2011 Feb 22;13(1):R30.E-pub). On this background there should be no offering of selection for types of research. Neither patients nor researchers know at the time of sampling for what good purpose the samples may be used. We suggest therefore that the appropriate term to be used is "broad consent for future research purposes" and this should be made explicit in Article 11. (BBMRI.SE / BBMRI.BE) *Discrepancies on this specific above proposal for modification* It is preferable not to quote broad consent as the model that should be used by any countries notably because ethical debates are still ongoing and because other mechanisms are currently being developed (e.g. multilayer consent, or dynamic consent processes, or information and non-opposition mechanisms). These mechanisms could present the same advantages than the so-called broad consent without adopting a broad approach by default. Furthermore, "broad consent" is not a recognised legal term and is not fully accepted by all jurisdictions. Thus, to date, it would be better to keep an objective/flexible wording, as proposed by the Council, as it allows many different and ethically sounded practices to develop, and does not orient legislators for adopting a particular and yet still debated method. (BIOBANQUES) **Proposals for specifications:** It should also be made explicit that each future research project should be approved by an ethical review board. Since the recommendation also involves previously collected samples, information and consent procedures should be

	specified for them as well, the two options generally used being opt-out or use without renewed consent, in both cases associated with approval by an ethical review board. **Proposals for specifications of the information to be provided:** The person concerned should always be informed about: - The way of how feed-back of incidental findings is managed. - The risk that he/she could be obliged to disclose any genetic risk-information he is aware of to e.g. insurances. Sequencing and genetic analyses require information and consent of the person. The information must address the risk of potential re-identification in the future, which will increase with technical progress. **Para.1** **Proposals for specifications:** It is not clear what is meant by "an intervention to be carried out to remove the materials". If this refers to the method of sampling, e.g. drawing blood or taking biopsies, the recommendation is redundant. Every individual is already by law protected against someone drawing blood or performing biopsies without his knowing and free consent. If "intervention" here means to say something more about the purpose of removing the samples and the need to be specific this is not possible for sampling done for future research purposes and would be counter productive for the fulfilment of rights of access to preventive health care and the right to benefit from medical treatment. **Proposals for minor textual modifications:** 1. Prior to requesting consent to remove human biological materials ("samples" or "resources" preferred, depending on the intended breadth given to these provisions) for storage for future research, the person concerned should be provided with comprehensible information: i. that is specific with regard to the intervention carried out to remove the biological materials; and ii. that is as precise as possible with regard to: - any research use foreseen; - the conditions applicable to the storage of the biological materials; and - any other relevant conditions governing the use of the materials. **Para. 2.** **Proposed add:** The persons concerned should also be informed of the rights and safeguards prescribed by law for their protection "as well as the means offered to effectively exercise their rights". **Para. 3.** Good ! **Proposed adds:** "The person concerned should be informed about the consequences that such offered choices could induce. Where relevant, the person concerned should also be informed about the potential costs related to the exercise of these choices". (BIOBANQUES)

	Proposal of specifications There is an indefinite number of potential choices and in reality not all of them can be implemented. It may be that if a person wants to limit the use of material to a certain type of research, the biobank cannot accept the material for storage. The possibility to choose (limit consent) may and should be given, but only if it is understood that limitation may in reality be equal to not giving a consent at all, and the actually available choices may be to participate or not. There should be no obligation for a biobank or a researcher to accept material they cannot reasonably use or when they cannot e.g. for practical or financial reasons reliably manage different types of consents. (BBMRI.FI) *Discrepancies on the above comments on para.3.* Not so good for prospective clinical studies because at any moment verification is necessary about whether the storage and use of materials complies with the choice expressed, with the consequence that clinical studies will be delayed, postponed or impossible. **Modifications proposal para 3:** - by analogy to the Belgian law - the persons (…) materials, as long as the use of the biological material in a research project has not been decided upon. Bad! For retrospective residual and studies based on residual material. In this context, at the moment of storage it is impossible to offer to the donor the possibility to precisely be informed of the aim of the future research. Nevertheless, general research information can be given by different ways (website, leaflets…). Moreover, all the studies are submitted for approval to the Ethical committees which guarantee the patient's rights. **Proposal of adds:** - by analogy to the Belgian law 2008 Art. 20. § 1 3rd paragraph – When it is impossible to ask authorisation for a "secondary" use or when it is exceptionally inappropriate, the biological material can be used based on an approval of an ethical committee. (BBMRI.BE). **Proposal for deletion** This is not useful. This Paragraph should be deleted. By doing this, we would be encouraging people to make choices they would probably never have asked for. It would only make information tracking more difficult and increase the likelihood of errors. A minefield of complexity, cost, potential for error and risk of harm to persons concerned. It is not clear what problem this paragraph is trying to solve. Some focus groups or studies may indicate that people would like to know how their samples are being used. For example on page 35 of the BBMRI ELSI WG "Biobanks and the Public", it is written: "On the issue of consent almost 7 in ten Europeans opt

	for specific permission sought for every new piece of research." It is not clear what "opt" means here, but even if this represents an unbiased, undirected and spontaneous preference, it is still not certain that it is in the best interests of research or of the persons concerned themselves to go down this road. A few persons might currently be lost by not offering this choice, but there is no evidence that this is a real problem nor that this paragraph would solve it if it existed. (IBBL – Integrated Biobank of Luxembourg) **Para. 4.** **Ask for specifications:** What is the meaning of "express"? Does that mean written? Does that mean informed? Does that mean actively opted-in (like explicit consent)? This term is subject to very different interpretations.
Article 12 – Removal of biological materials from persons not able to consent for storage for future research 1. Biological materials may only be removed for storage for future research from a person who, according to law, is considered not able to consent with the written authorisation from the representative or an authority, person or body provided for by law. The representative, the authority, the person or the body concerned should beforehand be given the information required by Article 11, paragraph 1, i and ii and paragraphs 2 and 3. 2. Persons not able to consent should be informed in a manner compatible with their understanding. An adult not able to consent should as far as possible take part in the authorisation procedure. The opinion of a minor should be taken in consideration as an increasingly determining factor in proportion to age and degree of maturity. Any objection by the person not able to consent should be respected. 3. Biological materials from persons not able to consent may only be removed for storage for future research having the potential to produce [real and direct benefit to their health or, in the absence thereof,] benefit to persons in the same age category or afflicted with the same disease or disorder or having the same condition. The removal should entail only minimal risk and minimal burden for the person on whom it is carried out.	**Para. 2.** **Last sentence:** is this covering the exercise of a right to withdraw from a person not able to give consent but who expressed its will towards a withdrawal?

4. Where a person not able to consent, from whom biological materials have been removed for storage for future research attains the capacity to consent, the consent of that person for continued storage and research use of his or her biological materials should be sought.	**Para. 4.** **Proposal of add:** Where it is impossible or inadequate to recontact the person or where this involves disproportionate efforts an approval from a competent Ethics Committee should be sought in order to continue the activities under the appropriate standards of protection.
Article 13 – Storage for future research of residual biological materials 1. Biological materials removed for purposes other than for storage for future research should only be stored for future research with the consent of the person concerned, provided for by law. This person should beforehand be given appropriate information, as referred to in Article 11, paragraph 1, ii. and paragraphs 2 and 3, including on the right to refuse. 2. Whenever possible, information as referred to in paragraph 1 should be given and consent requested before biological materials are removed. 3. Biological materials removed for purposes other than for storage for future research and already anonymised, may be stored for future research subject to authorisation provided for by law. Anonymisation should be verified by an appropriate review procedure.	**General Comments/Questions:** What about the possibility to obtain a permission/authorisation/approval from a competent Ethics Committee to requalify the samples for research uses? Is this covered by this article? Referral to national law for planning other legitimate grounds should be used. **We stress that is it absolutely necessary to be able to store also identifiable old samples in an appropriate manner under a governance for future research without a consent.** It seems possible under Article 17.2 to use samples for research without consent under certain procedure. Why not apply the same for storage? And if it has not been possible to store the samples due to lack of consent, how could one use them for research? Does this mean such samples that have not been stored, but exist e.g. in pathological archives? Is it then de facto a by-pass? Now this seems, that a person has to consent a) for storage under 13.1. **and** then b) separately for research under 17.1. This is not sensible or practical or does not even safeguard participants' interest. We suggest the Finnish model: broad consent for storage *and* use for future research within certain field of activities under a certain governance model; possibility to follow for which research samples and data have been used and right to withdraw. Research protocol specific consent is elementary in clinical trials, but *does not fit here*. (BBMRI.FI) *Discrepancies on this last proposal:* We agree about the main point stressed above. However, we oppose to the explicit quote of "broad consent" as the recommended model to use as it is, again, not officially recognised by all National Laws in Europe and there might be efficient and ethically less controversial alternatives in a near future. Thus, provided that appropriate governance policies are effective (referral to Chapter V could be done), that all the public authority/ethics committee authorisations have been obtained and that independent oversight is ensured, the storage for future research purposes should be valid, whatever the form of consent that has been used (broad or specific; opt-in/opt-out consent). (BIOBANQUES) **Para.1.** **Proposal for textual harmonisation:** "1. Residual identifiable biological samples…"

	Proposal for textual specifications What is consent under this text? Opt-out or non-opposition systems, are they considered as consent? In paragraph 1 consent seems not to require anymore to be "express". A definition of "consent" and "authorisation" would be very useful. We would prefer wording in the recommendation which explicitly says that the "opt-out" system (i.e. that, subject to information being readily available to persons concerned, consent for use of residual materials for future research will be assumed unless the persons take the initiative to opt out) is one legitimate way in which these recommendations could be implemented in member states. Old collections can be very large and it is unrealistic that all persons could be contacted directly. It is often not feasible to recontact the persons and may sometimes even be unethical (source of stress,…). Opt-out consent should be valid as well as opt-in. A public announcement mechanism with a possibility to object, and with Ethics Committee approval + official governmental authorisation (e.g. like in Finland), should be an option to avoid wasting important and valuable collections, which would be unethical. **Proposed Modifications:** "[…] should only be stored for future research with the presumed or explicit "consent of the person concerned. This modification is necessary to allow studies on residual biological material as provided under several National laws (E.g. Belgian, French laws). **Para. 3.** 3. Biological materials removed for purposes other than for storage for future research and already anonymised, may be stored for future research subject to authorisation provided for by law and notably in the respect of information and consent requirements. Anonymisation should be verified by any existing competent authority according to an appropriate review procedure.
Article 14 – Storage for future research of residual biological materials from persons not able to consent 1. Biological materials removed for purposes other than for storage fur future research from persons not able to consent should only be stored for future research with the authorisation from their representative or an authority, person or body provided for by law. The representative, the authority, the person or the body concerned should beforehand be given appropriate information, as referred to in Article 11, paragraph 1, ii. and paragraphs 2 and 3, including on the right to refuse. 2. Whenever possible, information as referred to in paragraph 1 should be given and	**Proposal of add:** Again, what about the possibility to obtain a permission/authorisation/approval from a competent Ethics Committee to requalify the samples for research uses? Is this covered by this article? This possibility should explicitly be recognised and mentioned in this article and throughout the recommendation; additional referral to national law for planning other legitimate grounds should also be used.

authorisation requested before biological materials are removed. 3. Biological materials removed for purposes other than for storage for future research from persons not able to consent may only be stored for future research having the potential to produce [real and direct benefit to their health or, in the absence thereof,] benefit to persons in the same age category or afflicted with the same disease or disorder or having the same condition. 4. Where a person not able to consent, from whom biological materials have been removed for purposes other than for storage for future research, attains the capacity to consent, the consent of that person for continued storage and research use of his or her biological materials should be sought. 5. Biological materials removed for purposes other than for storage for future research and already anonymised, may be stored for future research subject to authorisation provided for by law. Anonymisation should be verified by an appropriate review procedure.	**Para.3.** **When growing up children may benefit from sampling made when they were young** It is recommended that sampling from persons not able to consent must benefit persons in the same age. However, a growing body of data shows that health events early in life may affect adolescent and adult health. Other empirical studies support the hypothesis that epigenetic changes caused by environmental conditions early in human life can have effects throughout life. Because it is likely that genetic epidemiology will uncover more of these gene-environment interactions, it is essential that scientists with multiple backgrounds and expertise have access to samples and data that are representative of the different phases of life and that sampling can be done for children even when the benefits may come later. **Comment about "anonymisation"** Anonymised samples are often of limited value: why store samples that one cannot connect with any information or follow-up? Instead, it could be non-identifiable for the researcher, but a biorepository has to have a code key safely stored, for instance. Anonymisation does not allow for withdrawal of consent. If anonymisation is regarded as a panacea, what is then the purpose of this recommendation? Data protection is another thing and already strictly regulated. Use of anonymised data does not respect individual wishes and values. This is an ignored issue in policy papers which seem to reduce respect for self determination only to identifiable samples and data. **Para. 4.** **Proposal of add** Idem than for Art. 12.4: **"**Where it is impossible or inadequate to recontact the person or where it is involving disproportionate efforts an approval or a waiver from a competent Ethics Committee should be sought in order to continue the activities under the appropriate standards of protection". **Para. 5.** **Proposal for textual specifications** Biological materials removed for purposes other than for storage for future research and already anonymised, may be stored for future research subject to authorisation provided for by law and notably in the respect of information and consent requirements. Anonymisation should be verified by any existing competent authority according to an appropriate review procedure.

Article 15 – Biological materials removed after death 1. Biological materials should only be removed from the body of a deceased person for storage for future research with the consent or authorisation, provided for by law. This consent or authorisation should have been preceded by appropriate information, including on the right to refuse. 2. Biological materials should not be removed for storage for future research if the deceased person is known to have objected to it.	**Para.1.** **Proposal for textual changes** 1. Identifiable biological materials should only be removed from the body of a deceased person for storage for future research with the consent or authorisation, provided for by law. This consent or authorisation should have been preceded by appropriate information, including on the right to refuse. **Para.2.** **Proposal for textual changes** 2. Biological materials/resources (see comments above) should not be removed for storage for future research if the deceased person is known to have objected to it. The will of the person might be sought by consulting the closest having been able to be aware of the patient's own standpoint. **However,** – Biological material can be obtained during a post-mortem examination - as a diagnostic procedure performed by a pathologist in a hospital. This material becomes "residual material" and could be used for research purposes. The execution of a post-mortem examination is not (always) subjected to informed consent; (e.g. in Belgium, this is subject to presumed consent). – Similarly, biological material can be obtained when harvesting organs for transplantation. This article is in contradiction with the Belgian legal context.
Article 16 – Right to change the scope of, or to withdraw, consent or authorisation 1. When a person has provided consent to storage of identifiable biological materials for future research, the person should retain the right to withdraw or alter the scope of that consent. When identifiable biological materials are stored for research purposes only, the person who has withdrawn consent should have the right to have, in the manner foreseen by national law, the materials either destroyed or anonymised. The person who is considering withdrawing consent should be made aware of any limitations on withdrawal of his or her biological material. 2. The representative, authority, person or body provided for by law having given authorisation for storage for future research of biological materials removed from a person not able to consent, should have the rights referred to in paragraph 1. Where the person from whom biological materials have been removed attains the	**Para. 1.** **Proposal for textual specification:** When a person has provided consent to storage of identifiable biological materials for future research, the person should retain the right to withdraw or alter the scope of that consent at any time. When identifiable biological materials are stored for research purposes only, the person who has withdrawn consent should have the right to decide (in the manner foreseen by national law), whether the bio-materials shall either be destroyed or anonymised. (It should be made clear, however, that anonymisation is not a possibility to continue research with such materials because in the end the person has previously withdrawn consent). **Proposal for textual clarification :** Make two new paragraphs for the two last sentences as they are referring to different steps with respect to the right to withdraw. **Proposal adds:** the persons (…) materials, as long as the use of the biological material in a research project has not been decided upon.

capacity to give consent, that person should have the rights referred to in paragraph 1.	**Comment about "anonymisation" :** Withdrawal of consent should NEVER allow for further use of bio-materials/resources simply by "anonymisation" (against the will of the person concerned!). The anonymisation (-procedure) of meta data must be subject to the person's information/consent.
CHAPTER IV – Use of biological materials in a research project	**General comments :** **Scope:** Clarify the title/scope of this chapter (ref. « Further use of… », in accordance with exclusions of Article 2.2. **Research falling outside the scope of consent may be authorised by law** It is suggested as a general rule that research on biological materials should only be undertaken if it is within the scope of the consent or authorisation given by the person concerned (Article 17 para.1.). Everyone agrees that when someone has explicitly said no to a certain purpose or to other purposes than the one consented to, one should respect that. However, often the scope of the consent in association with previously collected samples is unclear, or just silent about possible purposes. Going back for a renewed consent has a cost in that there will be drop outs and many samples will not be used, thereby decreasing the scientific value of a study and therefore not fully respecting the rights of access to preventive health care and the right to benefit from medical treatment attainable through medical research. Regulatory frameworks usually assign to ethical review boards the right to select appropriate information and consent procedure, as well as the possibility to approve research without (renewed) consent (waiver). This circumstance should be clearly reflected in the recommendations. **Exemption clause:** The use and storage of material beyond the scope of the person's consent must be clearly limited to some defined exemptions and shall only be possible on the basis of national legislation assigning ethics committees the competence to scrutinize thoroughly any research beyond the consent of the donor, – without prejudice to other competences of ethics committees (art. 18).
Article 17 – General rule 1. Research on biological materials should only be undertaken if it is within the scope of the consent or authorisation given by the person concerned. 2. i. If the proposed use of identifiable biological materials in a research project is not within the scope of prior consent or authorisation, if any, given by the person concerned, consent or authorisation to the proposed use should be sought and, to this end, sufficient efforts should	**Para.1.** Including opt-out material. See comments under art.13.1. The term "person concerned" which is used in different contexts, should be clearly defined, as suggested above in the general comments as it is the subject of several important rights.

be made to contact the person concerned. The wish of the person concerned not to be contacted should be respected. ii. Where the attempt to contact the person concerned proved unsuccessful, these biological materials should only be used in the research project subject to independent evaluation of the fulfilment of the following conditions: *a.* evidence is provided that sufficient efforts have been made to contact the person concerned; *b.* the research addresses an important scientific interest and is in accordance with the principle of proportionality; *c.* the aims of the research could not reasonably be achieved using biological materials for which consent or authorisation can be obtained; *d.* there is no evidence that the person concerned has expressly opposed such research use.	**Para. 2.ii.** **Proposal for textual clarification :** To add « and » at the end of each letter (a; b; c; d). **Para. 2.ii.a.** What is evidence and what is sufficient -emails, phone records, registered letters...? This may lead to very different practices, propose to follow 22.1 of the current recommendation.
3. Anonymised biological materials may be used in a research project provided that such use does not violate any restrictions placed by the person concerned prior to the anonymisation of the materials and subject to authorisation provided for by law. Anonymisation should be verified by an appropriate review procedure. 4. Biological materials from persons not able to consent may only be used for research having the potential to produce [real and direct benefit to their health or, in the absence thereof,] benefit to other persons in the same age category or afflicted with the same disease or disorder or having the same condition.	**Para. 3.** **Proposal for textual changes** Anonymisation should be verified by any existing competent authority according to an appropriate review procedure. Depending on the meaning of "authorisation" we propose to add the sentence "This should not exempt from the other requirements provided by the law regarding independent ethical review". Last sentence: "technically verified by a competent authority". Does use of anonymised samples safeguard human dignity? Why build up a strict procedure for use of identifiable samples, but keep it light when anonymised? Is the recommendation mostly about data protection? Then it is unnecessary, as privacy regimes already exist as binding law. **Again "Anonymised":** There is no appropriate anonymisation of biological material/samples and anonymisation of the meta data requires **information and consent** of the donor in case the material is continued to be used after anonymisation, since it retails the loss of fundamental rights, e.g. the right of withdrawal. **Comment:** Para. 2. 3. And 4. are the responsibility of the competent Ethics Committee.

Article 18 – Independent review 1. Research should only be undertaken if the research project has been subject to an independent examination of its scientific merit, including assessment of the importance of the aim of the research, and verification of its ethical acceptability. National law may additionally require approval by a competent body. 2. Member states should apply the principles concerning ethics committees contained in chapter III of the Additional Protocol concerning Biomedical Research (CETS No. 195) to the review of the research project within the scope of this Recommendation. 3. Review procedures may be adapted to the nature of the research and the extent to which the persons from whom biological materials have been removed could be identified from these biological materials.	**General comment / Definitions** Does the term « approval » is different from the « authorisation » referred into this text? If it is, need to write approval in several articles (see above in general comments the need of definition). Some interpretations of "scientific" exclude research that eventually aim at commercial product/service/benefit (which many universities and research units want as well as companies). Commercially motivated research should be allowed (with appropriate information and consent procedures) to facilitate getting new innovations to the market. This is not to say that the research should not be made with valid scientific methods or that the results would not need to be made available. **Para. 1.** **Proposed specifications** Research should only be undertaken if the research project has been subject to an independent examination of its scientific merit, including assessment of the importance of the aim of the research, verification of its ethical acceptability and legal compliance. National law may additionally require approval by a competent body. **Para. 3.** **Proposal for textual clarification** Review procedures should be adapted to the nature of the research and the extent to which the persons from whom biological materials have been removed could be identified from these biological materials.
Article 19 – Availability of results 1. On completion of the research, a report or summary should be submitted to the ethics committee or the competent body. 2. Appropriate measures should be taken to make public the results of research in reasonable time.	**Para.1.** **Increasing bureaucracy for ERB's without any rationale / Ask for specification or deletion** It is suggested in article 19 that scientists should submit a report or a summary of the research results to the ethics committee. It is not at all clear what these committees should do with such a report and what use it may have. Ethics committees etc. /bodies may not have this kind of role and have no use for or power to react to any reports. EC/authority filing should not be used to legitimise not making results publicly available. Propose this to be deleted or at minimum include a reference e.g. "if so required under applicable law" or something similar or give the results back to the repository. (BBMRI.SE) *Discrepancies on this last proposal of deletion:* There is already a legal obligation for researchers to submit a report to the Ethical committee in several States (E.g. Belgium). (BBMRI.BE) **Para.2.** **Proposal for specification and harmonisation** This seems weak and not publishing results is a major ethical issue. WMA Declaration of Helsinki Art 36 states that

	"Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports." Propose the recommendation to be aligned with the declaration. Reference to reasonable time is good (and missing in the declaration). In addition, a credit should be made to the repository used in publication.
CHAPTER V – Governance of collections **Article 20 – General principles** 1. The person and/or institution responsible for the collection should be designated and this information should be publicly available. 2. The purpose(s) of the collection should be specified. The principles of transparency and accountability should govern its management, including, where appropriate, access to and use and transfer of its biological materials and disclosure of information. 3. Any change of purpose of a collection should be subject to independent examination and, where necessary, may require that appropriate consent or authorisation of the persons concerned be requested. 4. Each sample of biological material in the collection should be appropriately documented and traceable, including information on the consent or authorisation. 5. Quality assurance measures should be in place, including conditions to ensure appropriate security and confidentiality during establishment, use and, where appropriate, transfer of elements, of the collection. 6. Procedures should be developed for any transfer of the whole or part of the collection as well as for the closure of the collection; these should be in accordance with the original consent or authorisation. 7. Information about the management and use of the collection should be made available to the persons concerned and should be regularly updated, with a view to facilitating, where appropriate, the exercise of the rights laid down in Article 16. 8. The conclusions of the research should be made available to the persons concerned in reasonable time, on request.	**Para. 1.** **Proposal for textual changes** "The person and/or institution responsible" should be changed in "The person and the institution responsible", as person may change and the collection should always refer to the institution that has the final responsibility of the collection**.** **Para.2.** **Governance principles should apply also to broadly consented collections** In line with what has been argued above governance principles should not include requirements that the purpose of a collection should always be specified. **Para.6.** **Proposal for textual clarification** This paragraph should be divided in two distinct paragraphs to detail a little bit more, one for the question of transfers, the other for the question of collection/biobank closure. **Proposed add** …and for providing material for research from the biobank/collection. **Proposed textual changes:** …"should be made available on request to the persons concerned…" **Questions** Can we always anticipate the closure of a collection at the time of procurement (e.g. cohorts)? What to do in such a

9. Reports on past and planned activities, including information about access by third parties, should be published at least annually.	case? What kind of procedures "for the closure" of the collection should be developed? E.g. Procedures planning the fate of the stored and used human biological samples in case of definitive biobank closure / final stopping of biobank activities.
Article 21 – Individual feedback 1. Clear policies should be developed on feedback concerning findings that are significant for the health of the persons arising from the use of their biological materials. 2. Feedback should take place within a framework of health care or counselling. 3. The wishes of individuals not to be informed should be observed.	**Para. 1.** **Proposal for textual clarification** 1. Clear policies should be developed on feedback concerning results and/or incidental findings that are significant for the health of the persons arising from the use of their biological materials. Very good to require a policy, but not develop an obligation. **Para. 2.** **Proposed add:** Important to add something like only validated and clinically actionable results can be communicated. In addition, research biobanks and clinical biobanks have different capacities. **Para. 3.** **Proposal for textual modification** The subject of return of results is fashionable and the dust has not settled on "best practice", if it ever will. For example there is a current line of thought, which says that if the information is actionable, the donor must be informed even if he has asked not to be, as it is unethical to stay silent when you know that specific personalized action could be taken to reduce serious health risks to an individual. No shortage of experts will argue the contrary. The point here is not to say who is right, just to say that there is no agreement today on best practice, certainly not on the one recommended in this paragraph. We recommend changing this paragraph to say that the policy of the collecting organization with respect to return of results must be clearly stated in subject information sheets at the time of consent.
Article 22 – Access 1. Clear conditions governing access to, and use of, biological materials should be established. 2. Member states should take measures to facilitate appropriate access by researchers to collections of biological materials. 3. Transparent access policies should be developed and published, including arrangements for oversight of access and transfer procedures. 4. Appropriate access mechanisms should be	

developed to maximise the value of collections. These should include traceability of the uses granted by the collection.	
Article 23 – Transborder flows 1. Biological materials should only be transferred to another state if a comparable level of protection is either ensured by the law of that state or by legally binding and enforceable instruments adopted and implemented by the persons involved in the transfer and further processing. 2. The transfer of the biological materials should be done under appropriate safety and confidentiality conditions. 3. A documented agreement between the sender of the biological materials, on the one hand, and the recipient, on the other, should be signed. Appropriate consent or authorisation, including, where appropriate, any relevant restriction established by the person concerned, should be included in the agreement.	**Proposal for an add into paragraph 2** "Biological material should only be transferred under the highest level of protection adopted between the two states". E.g: Dengue virus is BSL3 in France, whereas BSL2 in UK. Transfer from France can only be done if the UK end-user owns a BSL3 facility. **Proposal for two new paragraphs 4 and 5** 4. All the necessary measures should be taken to document and ensure the traceability of the transfers. 5. Transfers should not result in the impossibility for the person concerned to exercise its rights pursuant to applicable law. Appropriate measures should be planned within the transfer agreement.
Article 24 – Oversight 1. Any proposal to establish a collection of biological materials should be subject to an independent examination of its compliance with the provisions of this Recommendation. 2. Each collection should be subject to independent oversight which is proportionate to the risks involved for the persons whose biological materials are stored in the collection. Such oversight should aim in particular at safeguarding the rights and interests of the persons concerned in the context of the activities of the collection. 10 Oversight mechanisms should cover, at a minimum: i. the implementation of security measures and of procedures on access to, and use of, biological materials; ii. the publication of reports on past and planned activities, including information about access by third parties, at least	**Para.1.** **Proposed add** ...as reflected in the applicable law" - the recommendation cannot override legislation. **Para. 2.** **Proposal for textual changes** i. security, confidentiality measures… **Concern :** ii. the publication of reports on past and planned activities, including information about access by third parties, at least annually; This kind of rule could lead to violate confidentiality in the context of partnerships with thirds. Concerned persons are informed about the possibility of thirds to access their human biological resources but what is the meaning of publishing this information, and to what extend this can be useful. **Proposal for textual changes** ii. …and transfers at least annually.

annually; iii. the change in the risks to persons whose biological materials are stored in the collection and, where appropriate, revision of policies; iv. appropriate information to the persons concerned of changes in the management of the collection in order to be able, where appropriate, to exercise the rights laid down in Article 16; and v. the development and implementation of feedback policies, including regular review. Oversight mechanisms should be able to adapt to possible evolutions of the collection and of its management.	
CHAPTER VI – Re-examination of the Recommendation **Article 25 – Re-examination of the Recommendation** This Recommendation should be regularly re-examined after its adoption, notably in the light of the experience acquired in the implementation of its guidelines.	