
HOW-TO GUIDE:

NEXT GENERATION BIOBANKING/BIOBANKING WITH THE NEXT GENERATION

INTRODUCTION

It has long been well established that the availability of an extensive, systematic collection of human samples (both diseased and healthy) with well-documented phenotypic data is a crucial requirement for developing and strengthening precision and preventive medicine. Advanced science and tailored medicine need a global, integrated data based on translational biobanking. Biobanking global data (biological, omics, profiling, interfamilial and intergenerational data) over time implies participation and engagement and defines new frontiers of scientific citizenship.

“Omics, artificial intelligence (AI) driven process automation, data analytics, robotics, the internet, and other emerging technological advances are driving the revolution of biospecimen science, both providing new insights into the genetic component of human disease and developing a more personalised approach to healthcare.”¹

Integrating and digitalising real-world data and biobanked samples with data correlated and improved by omics, AI/machine learning technologies produce a shift in science and society, creating a revolution. The translational biobanking/medicine, with its digitalisation, can be our training ground to identify the impact of this shift on ethical, legal, and societal practices and to rethink the risk assessment accordingly, in relation to ethical review, informed consent/assent, and oversight governance processes within a Responsible Research and Innovation (RRI) framework aimed at promoting a democratic (inclusive, transparent, accountable) governance of science and innovation. It is a challenge that broadly impacts and concerns every person. No wonder that the Nature editorial on the Cambridge Analytica personal data controversy firmly stated that *“Academics across many fields know well how technology can outpace its regulation. All researchers have a duty to consider the ethics of their work beyond the strict limits of law or today’s regulations. If they don’t, they will face serious and continued loss of public trust.”²*

The ‘next-generation’ biobanking model may overturn the guarantees and the participatory practice we identified from the Nuremberg Code to today: it is a driving force not only for Precision Medicine but also for Predictive Medicine, introducing the need for new rights such

¹ Casati, S., and B. Ellul "ELSI Challenges with Children in Translational Medicine." IntechOpen (2024). <https://doi.org/10.5772/intechopen.1002550>.

² "Cambridge Analytica Controversy Must Spur Researchers to Update Data Ethics." [In eng]. Nature 555, no. 7698 (Mar 29 2018): 559-60. <https://doi.org/10.1038/d41586-018-03856-4>. <https://www.ncbi.nlm.nih.gov/pubmed/29595795>.

as the right to an open future for the children as well as the right of reasonable interferences, especially regarding predictions drawn from big data analytics with low verifiability. So as not to reduce the consent to a farce and to enable every citizen to consciously act and engage within a dynamic complex scientific environment, innovative, responsible, and participatory assenting/consenting models are required; assenting/consenting models must be capable of time travel, just as data are capable of time travel and must be closely in dialogue and structured according to the governance. Conscious that the real game is played by triangulating a renovated across-time role of the third-party bodies such as Ethics Committees, biobank-registries, and Access Committees, systemic oversight governance should be based on reflexivity, inclusivity, and responsiveness, that should include all social actors, first and foremost citizens, and a multi-actor engagement action to redress power asymmetries, to avoid a slippery slope but also to evade double discrimination, both as a consequence of real-world-global data-driven research and a not-inclusion in research.

The impact and implications of the paradigm shift with the technologization of science, biobanking (next-generation biobanking), medicine, and de facto of health, as well as the RRI challenge at stake, concern first and foremost the next-generation, future citizens, future researchers. The next generation, both as future citizens and potential scientists, and researchers, are at the forefront of the development, sustainability, and equity of Translational Medicine, requiring an extended scientific community, which recognises and includes both citizens and the clinicians as partners, and regenerates research as a responsible participatory process.

The sample-and-data-based translational research is a challenging training ground to empower children to be conscious of their rights to take part proactively in research processes and make informed decisions about their own health. The research ecosystem should fully evolve into a participatory scientific ecosystem that guarantees the setting and tools to recognise and include the next generation not merely as research participants, but also as actively engaged and empowered RRI actors who have a deep knowledge and understanding of their rights to health and science as contributors to translational medicine and biobanking participants.

Consequently, we promote a glossary of terminologies and concepts relevant for biobanking with and for the next generation along the following categories:

- The actors
- The context
- The assenting/dissenting process
- Special rights
- Potential risks
- Good practices for risk assessment
- Participatory framework

GLOSSARY

The Actors

Adolescent:

A human being “between childhood and adulthood, from ages 10 to 19. It is a unique stage of human development and an important time for laying the foundations of good health. Adolescents experience rapid physical, cognitive and psychosocial growth. This affects how they feel, think, make decisions, and interact with the world around them.”³

Child:

“Every human being below the age of eighteen years unless under the law applicable to the child, majority is attained earlier.”⁴ The term is used when discussing paediatric research and ethical issues in research with children, to distinguish it from the term minor with more legal connotations.

Minor:

A person below the legal age of majority or adulthood, as stipulated by the laws of their respective jurisdiction. The term is used in legal contexts to denote a person not having the full legal rights and responsibilities of adulthood.

Mature minor:

A person below the legal age of majority who has the necessary understanding and decisional capacity to give ethical consent and make their own health care choices independent of their parents' or guardians' wishes. Ethical decisions regarding informed consent and confidentiality should be distinguished from legal requirements.

Emancipated minor:

A person below the age of majority (usually 18) who is considered legally capable. Depending on the state, emancipated minors are those who are already married, or pregnant or who belong to the armed forces or who have obtained an emancipation decree from the court.

Vulnerable persons in research:

Persons who, due to an intrinsic or situational condition, are placed at greater risk of being utilised in ethically inappropriate ways in research.

In general, “persons are vulnerable in research either because they have difficulty providing voluntary, informed consent arising from:

- limitations in decision making capacity (as in the case of children) or
- situational circumstances (as in the case of prisoners) or
- because they are especially at risk for exploitation (as in the case of persons who belong to undervalued groups in our society)”⁵

³ WHO. Adolescent health. https://www.who.int/health-topics/adolescent-health#tab=tab_1.

⁴ United Nations, Convention on the Rights of the Child, adopted and opened for signature, ratification and accession by General Assembly Resolution 44/25 of 20 November 1989, entry into force 2 September 1990, in accordance with Art.49.

⁵ US National Bioethics Advisory Commission (2001) Ethical & policy issues in research involving human participants. Bethesda, Maryland, 2001:85.

Child as a vulnerable in transition:

A child is a person in evolution with transitory/temporary vulnerability “...entitled to special care and assistance”⁶ because of the risk of subordination, due to the differential power relationships between adults (researchers, parents, guardians) and child participant, with a risk of manipulation in interaction with adults. The child is mostly exposed to the vulnerability by an opposite condition:

- potential discrimination (exclusion of children with disabilities, refugees, orphans,...)
- overprotection (without research specific to minors, they would suffer from the lack of development of tailored diagnosis and treatments).

The vulnerability, in this regard, does not arise from registered/diagnosed disorders or predisposition of a child, except in specific cases; it is rather a temporary vulnerability that can be exacerbated if the ecosystem (researchers, parents, guardians, etc.) would not recognise them as a human to respect, to listen to, or take their will into consideration. The participation of young people in all aspects of their personal and social development is a fundamental right; the ethical-legal-societal challenge is to guarantee and provide capability/empowerment and inclusive environments to equip children, but also adults, to ensure children’s participation in the healthcare and research knowledge and decision making.

Participant:

An individual who takes part in biomedical research, across translational processes, appropriately informed and engaged in research processes, enabling them to act proactively and consciously.

Parent:

A person who is legally responsible for a young human being, whether that relationship came to be through birth or legal means. A young human being can have up to two legal parents. In most European countries, parents exercise the responsibility jointly.⁷

Guardian:

A person appointed by the court as being legally responsible to make decisions on behalf of a minor when their parents are incapacitated or deceased or if the minor's parents are deemed unfit/cannot properly manage to ensure their child's safety and well-being.

“Professional trained or experienced in working with children”⁸:

Researchers, clinicians, psychologists, etc., specifically trained to listen to, inform and engage children in scientific research processes, as well as to assess their maturity.

Community of practice (CoP):

Groups of people who share an interest, a concern and/or a vision in something they do, and learn to do it better, while interacting regularly.⁹ Among the main characteristics distinguishing a CoP from any other group is the presence of a domain that unites all its members, who take collective responsibility for managing the knowledge they need to learn and share, to enable them to develop new practices, create new knowledge, and define new territory, together, on an ongoing basis.

⁶ UN (1948) Universal Declaration of Human Rights; Charter of Fundamental Rights of the European Union (2000/C 364/01).

⁷ https://europa.eu/youreurope/citizens/family/children/parental-responsibility/index_en.htm

⁸ EU Regulation 536/2014. Art.32.

⁹ Wenger, E. (1998) Communities of Practice: Learning, Meaning, and Identity. Cambridge: Cambridge University Press (Learning in Doing: Social, Cognitive and Computational Perspectives).

The Context

Biobanking:

The process of collecting, processing, storing, and distributing biological samples and associated data, while respecting the rights as well as the assent/consent of all participants involved, based on transparency, reciprocity, and inclusion.

Biobanking with children:

Step-by-step participatory, responsible research process recognising and including the child as the primary participant, not the parents/guardians who are in turn the gatekeepers, based on progressive young people's involvement in biomedical research, translational projects, and healthcare decision-making. Young people's progressive participation and engagement are systematically foreseen and supported including their views and experiences, within a new goal of promoting research with and for them, designed specifically for children/adolescents. Their involvement and engagement imply a change of pace, a transformation in biobanking settings and practices, which is fundamental to responsible biobank-based-research. Several mechanisms need to be implemented in biobanking with children, such as continuous re-evaluation and enhancement of the research process to incorporate children's evolving capabilities and viewpoints, training programmes for researchers on how to effectively communicate to children, adjusting assent processes, collecting feedback from children and ethical oversight, ensuring that their participation is both meaningful and ethically robust.

Paediatric biobanking:

The systematic collection, storage, distribution and use of biological materials and related data (biobanking) from young humans with an already diagnosed disease or who are undergoing clinical diagnostic investigations. The adjective 'paediatric' is a clinical term that directly situates biobanking in the clinical, diagnostic, and treatment context.

'Next-generation' biobanking:

A biobanking process based on new genomic technologies and supported by bioinformatics expertise, including AI/machine learning, but also transitioning from storing and distributing samples to enabling federated data repositories with potential improvement in healthcare for the next generation of future citizens and researchers. Its development and implementation are responsibly conducted if based on a step-by-step engagement process within an RRI framework with special attention to open access, participatory governance, sustainability, social justice, and inclusion.

Translational Medicine (TM):

*"[...] an inter-disciplinary branch of the biomedical field supported by three main pillars: bench side, bedside, and community. The goal of TM is to combine disciplines, resources, expertise, and techniques within these pillars to promote enhancements in prevention, diagnosis, and therapies."*¹⁰

Research biobank:

A service infrastructure, not for profit, established in a public or private institution and officially recognised by the competent authorities, which, in full respect of the rights of the participants involved, guarantees, and manages, according to international proven quality standards, the stable and continuous collection, preservation, and distribution of human biological materials and associated data for future research and ultimately for clinical care.

¹⁰ Translational Medicine definition by the European Society for Translational Medicine (2014) in New Horizons in Translational Medicine. <https://eutranslationalmedicine.org/translational-medicine-definition>

The biobank performs a public, custodian service, third-party function, guaranteeing the integrity of the biobanking process for all the actors involved and for society: the sharing of the biobanked samples, and the results is central to the entire activity of a research biobank and underscores the research biobank's purpose to advancing scientific understanding and improving public health outcomes.

Paediatric biobank or a biobank with a paediatric focus:

A biobank that collects samples from children with specific paediatric conditions, such as congenital disorders and rare diseases, and would follow the children over several years until adulthood, thus amassing a wealth of developmental, genotypic, and phenotypic data and enabling large cohort studies¹¹. Paediatric biobanks do also collect from healthy children for controls.

The Assenting/Dissenting Process: From Assent to Ethical Consent, to Consent on Attaining the Legal Age

"Before undertaking research involving children and adolescents, the researcher and the research ethics committee must ensure that:

- *a parent or a legally authorised representative of the child has given the permission; and*
- *the agreement (assent) of the child or adolescent has been obtained in keeping with the child's or adolescent's capacity, after having been provided with adequate information about the research tailored to the child's or adolescent's level of maturity."*¹²

Dissent:

*"When a potential research subject who is deemed incapable of giving informed consent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorised representative. The potential subject's dissent should be respected."*¹³

*"[...] the explicit wish of a minor who is capable of forming an opinion and assessing the information referred to in Article 29(2) to refuse participation in, or to withdraw from, the clinical trial at any time, is respected by the investigator;"*¹⁴

*"[...] If the person not able to consent is a minor, his or her opinion should be taken into 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. Any wishes previously expressed by such a person should be taken into account."*¹⁵

Informed assent:

A practical participatory process signifying an agreement by a child to participate in research, based on comprehensive, concise, clear, relevant, and understandable information, age-tailored for the child, provided by investigators or members of the investigating team who are trained or experienced

¹¹ Casati, S., B. Ellul, M. T. Mayrhofer, M. Lavitrano, E. Caboux, and Z. Kozlakidis. "Paediatric Biobanking for Health: The Ethical, Legal, and Societal Landscape." [In eng]. *Front Public Health* 10 (2022): 917615. <https://doi.org/10.3389/fpubh.2022.917615>. <https://www.ncbi.nlm.nih.gov/pubmed/36238242>.

¹² CIOMS & WHO (2016) Guideline 17 – Research involving children and adolescents in International Ethical Guidelines for Health-related Research Involving Humans: 65. <https://doi.org/10.56759/rgxl7405>

¹³ WMA (2013) Declaration of Helsinki, Art.29.

¹⁴ Regulation EU 2014/536 on clinical trials on medicinal products for human use, Art. 32.1 (c)

¹⁵ Council of Europe. Recommendation CM/Rec(2016)6 on research on biological materials of human origin, Council of Europe. Art.12.4.

in working with children.

This is a dynamic and continuous process based on an ongoing dialogue between children, parents and researchers/biobankers, from the biobanking proposal until the reuse and secondary use as well as access to the data and the results; “[...] *the child or adolescent is meaningfully engaged in the research discussion in accordance with his or her capacities. Assent must be considered as a process and is not merely the absence of dissent.*”¹⁶

Informed (ethical) consent (consenting):

A participatory, informed, dynamic process where the young human expresses a voluntary, informed choice due to maturity and evolving/refining of their capabilities of “(1) *understanding the information relevant to make a decision; (2) appreciating how the decision will impact them personally; (3) manipulating the information rationally and reasoning, and (4) communicating a voluntary choice*”¹⁷ The information provided should include risks, benefits, and ethical issues, such as their rights.

This choice meets the ethical requirements of full ethical consent when recognised and upheld by national legislation.

Consent to data processing:

Consent is one of the mechanisms that may be applied as a legal basis for lawful data processing as regulated by Articles 6(1)(a) and 9(2)(a) of the Regulation (EU) 2016/679 (GDPR). Article 4(11) of the GDPR defines consent of the data subject as “*any freely given, specific, informed and unambiguous indication of the data subject’s wishes by which he or she, by a statement or by a clear affirmative action, signifies agreement to the processing of personal data relating to him or her*”.¹⁸

The GDPR sets down the required information that must be provided about the nature and the purpose of the data processing, and the rights of the participant.

Legal consent on attaining the legal age:

The choice to take part in research or healthcare processes formally expressed by the minor on attaining the legal age; this consent has a legal weight, no longer needing the parent/guardian’s authorisation (consent). The legal age varies between countries but may also vary between consent to research participation and consent to medical intervention, even in the same nation.

‘Re-consent’:

The process of obtaining a renewed consent from participants to research biobanking when there are significant changes to the research protocol (such as new research purposes and/or uses are proposed to the research participant) or when new information about risks becomes available.

Age-tailored information to data processing:

“[...] *any information and communication, where processing is addressed to a child, should be in such a clear and plain language that the child can easily understand.*”¹⁹

Information and any communication “relating to processing should be provided “*in a concise,*

¹⁶ CIOMS & WHO (2016) Guideline 17 – Research involving children and adolescents in International Ethical Guidelines for Health-Related Research Involving Humans: 67. <https://doi.org/10.56759/rgxl7405>.

¹⁷ McGregor, K. A., and M. A. Ott. "Banking the Future: Adolescent Capacity to Consent to Biobank Research." [In eng]. *Ethics Hum Res* 41, no. 4 (Jul 2019): 15-22. <https://doi.org/10.1002/eahr.500023>. <https://www.ncbi.nlm.nih.gov/pubmed/31336038>.

¹⁸ Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) [2016] OJ L 119/1.

¹⁹ GDPR, Recital 58.

transparent, intelligible, and easily accessible form, using clear and plain language, in particular for any information addressed specifically to a child. The information shall be provided in writing, or by other means, including, where appropriate, by electronic means.”²⁰

Capability:

The quality or state of being capable, that is having attributes (such as physical or mental power) required for performance or accomplishment.²¹

(Legal) Maturity (Majority):

The age at which a person becomes an adult and acquires legal responsibility and the right to vote, be elected, or issue or sign legal instruments.

Legal capacity:

The capacity of a natural person to perform legal acts, i.e., to dispose of his or her rights and assume obligations. Legal capacity to act is acquired upon reaching the age of majority.

Special Rights (& Corresponding Duties and Responsibilities)

The long ELSI path of recognising the child as an evolving person who is guaranteed both the practical conditions and the development of capacities to participate in the processes that affect them, to which the child can contribute, and which may have an impact on their life and future choices, is a path of regeneration or absolute generation of rights, of special rights. These rights can be considered "special" both because they are structured on the basis of the uniqueness of the child, an evolving, learning person who, as he or she grows, strengthens their capacity to participate and determine their own decisions, and because they are rights that guarantee and promote the recognition of the child as a person capable of self-determination and participation.

These rights are 'special' also because they are mainly set out in Soft Laws, from the Belmont Report to the Oviedo Convention, from the Convention on the Rights of the Child to the Recommendation on the Participation of Children and Young People: from an ethical-legal-social point of view, soft laws bet on accountability processes and good practices by designing and imagining a framework of respect, equity, and dignity in practice.

This ethical (normative) framework is based on the practical engagement and commitment of all parts involved; within an RRI horizon, these rights can and must be reviewed by evaluating and verifying their grip as well as the conditions that make them claimable, as the Council of Europe stipulates in its Strategy for the Rights of the Child (2022-2027).²²

Right to be respected:

“Respecting persons [...] is often a matter of balancing competing claims”²³, of weighting autonomy against protection, with researchers working together with all the actors at stake, beginning from the potential participants. “Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them [...]”; For these persons

²⁰ GDPR, Art.12(1).

²¹ <https://www.merriam-webster.com/dictionary/capable>

²² Council of Europe (2022) Strategy for the rights of the Child. <https://rm.coe.int/council-of-europe-strategy-for-the-rights-of-the-child-2022-2027-child/1680a5ef27>.

²³ Basic Ethical Principles, 1. Respect for Persons. In Belmont Report, Ethical Principles and Guidelines for the Protection of Human Subjects of Research, 1979.

(immature), however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research.²⁴

Right of the child to be listened to and taken seriously:

“1. States Parties shall assure to the child who is capable of forming his or her own views the right to express those views freely in all matters affecting the child, the views of the child being given due weight in accordance with the age and maturity of the child.

2. For this purpose, the child shall in particular be provided the opportunity to be heard in any judicial and administrative proceedings affecting the child, either directly, or through a representative or an appropriate body, in a manner consistent with the procedural rules of national law.”²⁵

Right to freedom of expression:

“The child shall have the right to freedom of expression; this right shall include freedom to seek, receive and impart information and ideas of all kinds, regardless of frontiers, either orally, in writing or in print, in the form of art, or through any other media of the child's choice.”²⁶

Right to participate:

“The right of children and young people to participate applies without discrimination on any grounds [...] Consideration needs to be given to the notion of the evolving capacities of children and young people. As children and young people acquire more capacities, adults should encourage them to enjoy, to an increasing degree, their right to influence matters affecting them.

Particular efforts should be made to enable participation of children and young people with fewer opportunities, including those who are vulnerable or affected by discrimination, including multiple discrimination [...] In order to be able to participate meaningfully and genuinely, children and young people should be provided with all relevant information and offered adequate support for self-advocacy appropriate to their age and circumstances. If participation is to be effective, meaningful and sustainable, it needs to be understood as a process and not a one-off event and requires ongoing commitment in terms of time and resources [...]. Children and young people should always be fully informed of the scope of their participation, including the limitations on their involvement, the expected and actual outcomes of their participation and how their views were ultimately considered.”²⁷

Right to participate in all the decisions regarding health:

The Steering Committee for Human Rights in the fields of Biomedicine and Health at the Council of Europe has recently prepared the Guide to Children’s Participation in the Decision-making Process on Matters Regarding their Health²⁸, containing principles and good practices, to drive the manner of involving children in medical decision making. There are changes in the general perception of the autonomy and protection of children regarding their capacity to participate in decision-making. However, on matters concerning their health and general well-being, there is uncertainty as to how

²⁴ Synopsis from Part B: Basic Ethical Principles 1. Respect for Persons. In: Belmonte Report, Ethical Principles and Guidelines for the Protection of Human Subjects of Research, 1979.

²⁵ UN (1989). Convention on the Rights of the Child. Art.12.1.2.

²⁶ UN (1989). Convention on the Rights of the Child. Art.13.1.

²⁷ Council of Europe. Recommendation CM/Rec(2012)2 of the Committee of Ministers to member States on the participation of children and young people under the age of 18. Section II. Principles.

²⁸ Council of Europe. Guide to children’s participation in the decision-making process on matters regarding their health. April 2024. [https://www.coe.int/en/web/bioethics/guide-to-good-practice-concerning-the-participation-of-children#%2267269019%22:\[0\]](https://www.coe.int/en/web/bioethics/guide-to-good-practice-concerning-the-participation-of-children#%2267269019%22:[0]).

the increased recognition of their decision-making capacity should be addressed.²⁹

Right to an open future:

"Refers to the idea that children will become autonomous once they reach the age of majority, and therefore parents' decisions should be such as to ensure an autonomous choice when they are ready."^{30,31}

Right to the return of results:

*"Clear policies should be in place regarding feedback of health-relevant results to individuals obtained through the use of their biological materials, including for individuals who by law, do not have the capacity to consent."*³²

Right not to know one's genetic status:

*"Everyone is entitled to know any information collected about his or her health. However, the wishes of individuals not to be so informed shall be observed."*³³ The Explanatory Report to the Oviedo Convention adds that *"patients may have their own reasons for not wishing to know about certain aspects of their health."*³⁴ *"The right of each individual to decide whether or not to be informed of the results of genetic examination and the resulting consequences should be respected."*³⁵

Rights and duties of the parents (or legal guardians) to provide direction to the child in the exercise of their right:

*"States Parties shall respect the rights and duties of the parents and, when applicable, legal guardians, to provide direction to the child in the exercise of his or her right in a manner consistent with the evolving capacities of the child."*³⁶

Parents'/carers' responsibility to guarantee the right to participate:

*"Parents and carers have the primary responsibility for the upbringing and the development of the child and, as such, play a fundamental role in affirming and nurturing the child's right to participate, from birth onwards."*³⁷

Protecting the right to participate

"In order to protect the child or young person's right to participate, Member States should:

- *provide the greatest possible legal protection for children and young people's right to participate,*

²⁹ Council of Europe. Strategy for the rights of the child (2022-2027) March 2022. <https://www.coe.int/en/web/children/strategy-for-the-rights-of-the-child>.

³⁰ Casati, S., B. Ellul, M. T. Mayrhofer, M. Lavitrano, E. Caboux, and Z. Kozlakidis. "Paediatric Biobanking for Health: The Ethical, Legal, and Societal Landscape." [In eng]. *Front Public Health* 10 (2022): 917615. <https://doi.org/10.3389/fpubh.2022.917615>. <https://www.ncbi.nlm.nih.gov/pubmed/36238242>.

³¹ Feinberg, J. "The Child's Right to an Open Future." In *Philosophy of Education: An Anthology*, edited by Randall Curren: Wiley-Blackwell, 2006.

³² Council of Europe. Recommendation CM/Rec(2016)6 on research on biological materials of human origin, Council of Europe. Art.17.1.

³³ Council of Europe (1997). Convention on Human Rights and Biomedicine. Art.10.2.

³⁴ Council of Europe (1997). Explanatory Report to the Convention on Human Rights and Biomedicine. Paragraph 67.

³⁵ UNESCO (1997). Universal Declaration on the Human Genome and Human Rights. Art.5c.

³⁶ Convention on the Rights of the Child (1989). Art.14.2.

³⁷ Council of Europe. Recommendation CM/Rec(2012)2 of the Committee of Ministers to member States on the participation of children and young people under the age of 18. Section II. Principles.

- including in constitutions, legislation and regulations;*
- *undertake periodic reviews of the extent to which children and young people's opinions are heard and taken seriously in existing legislation, policies and practices and ensure that in these reviews, children and young people's own assessments are given due weight;*
 - *[....]*
 - *take a co-ordinated approach to strengthening children and young people's participation and ensure that participation is mainstreamed in decision- and policy-making structures;*
 - *allocate adequate financial resources and secure competent human resources to support children and young people's participation in both formal and informal settings.”³⁸*

Potential Risks

Therapeutic misconception:

Usually attributed to the research participant who fails to appreciate the difference between treatment and involvement in a research study or who believes that they will invariably benefit from the research. Vulnerable individuals, such as children and their families, may experience high expectations for clinical improvement because of clinical trial participation. This is often the case for participants who suffer from a disease for which there is no cure and/or specific treatment available.

Risk of conditioning and manipulation:

This is due to the differential power relationships between adults (researchers, guardians) and the child participant. Power imbalances may relate to age, intellectual ability, knowledge, relationship with the child, experience, and gender. Children are taught to respect and obey adults and that adults are wiser and have authority over them.

Risk of overprotection:

Categorising children as vulnerable under all circumstances³⁹ creates a potential slippery slope of overprotection to exclude them from research because it is considered too risky by the guardian(s) or too complex to handle by the researchers, especially for the ELSI challenges implied.

Risk of discrimination:

This occurs with the exclusion of children with disabilities, refugees, orphans, and others because of their conditions and/or circumstances.

Good Practices for Risk Management

Minor maturity assessment:

A professional assessment process aimed at evaluating the capacity/capability of understanding, handling the impact and rationale of the proposal, and communicating their voluntary choice, mainly based on: discussion with both the parents and child to gauge maturity/cognitive ability; feedback to assess understanding; use of general development, age cut-offs or a standardised tool, like the

³⁸ Ibidem. Section III. Measures.

³⁹ Coyne, I., A. Amory, G. Kiernan, F. Gibson. "Children's Participation in Shared Decision-Making: Children, Adolescents, Parents and Healthcare Professionals' Perspectives and Experiences." *European Journal of Oncology Nursing* 18, no. 3 (2014): 273-80. <https://doi.org/https://doi.org/10.1016/j.ejon.2014.01.006>. <https://www.sciencedirect.com/science/article/pii/S1462388914000155>.

modified MacArthur Competence Assessment Tool for Clinical Research MacCAT-CR.⁴⁰

Vulnerability mitigation:

The application of specific practices to make sure children and young people's vulnerability is mitigated in research, such as:

- working in partnership with children, young people, and parents/guardians,
- involving children, young people, and parents in the design of their research from the beginning, to improve awareness and perception of security and protection.

Moreover, as suggested by the Barcelona Declaration and the Belmont Report, this includes:

- not merely non-interference with the autonomy, dignity, or integrity of beings, but also
- that they receive assistance to enable them to realise their potential.

Finally, considering the RRI – Responsible Research & Innovation principle 'social justice and inclusion', avoids unfair exclusion of particular groups from either participation in research and/or access to benefits arising from research.

Children friendly tools/Age-tailored paths:

Tools co-designed and developed together with children, starting from their informational needs, with consideration of their evolutionary cognitive, psychological, and emotional state. Both the tools and paths are aimed at empowering and equipping children to act as active participants in research processes.

(Biobank) Custody:

This is the responsible caring process of biological samples and associated data, exercised by biobank personnel throughout the biobanking period, from collection to scientific use of the samples/data. It is based on the assent/authorisation given by the subject from whom the samples/data are collected and by the legal consent of the subject's guardian(s). Responsible custody requires careful governance and transparent policies to ensure the long-term physical quality of samples and the integrity of associated data, the privacy and specific rights of research participants, the confidentiality of associated data and the appropriate use of samples and data. Crucial to the full implementation of safekeeping is public and transparent access to governance documents and rules to ensure the quality of biobanking and to show respect for participants' rights.

Participatory Framework

"If biobank research is open-ended and ongoing then information technologies offer the possibility for participant involvement similarly to extend through time. Individuals need no longer be passive human 'subjects' but can be engaged over time and recognised as active, interested and valued research participants."⁴¹

"Children are not small adults who can be treated as though they were, and neither are they uniformly vulnerable beings who need protection; rather they are individuals in transition whose growth into

⁴⁰ Hein, I. M., M. C. De Vries, P. W. Troost, G. Meynen, J. B. Van Goudoever, and R. J. Lindauer. "Informed Consent Instead of Assent Is Appropriate in Children from the Age of Twelve: Policy Implications of New Findings on Children's Competence to Consent to Clinical Research." [In eng]. *BMC Med Ethics* 16, no. 1 (Nov 09 2015): 76. <https://doi.org/10.1186/s12910-015-0067-z>. <https://www.ncbi.nlm.nih.gov/pubmed/26553304>.

⁴¹ Kaye, J., E. A. Whitley, D. Lund, M. Morrison, H. Teare, and K. Melham. "Dynamic Consent: A Patient Interface for Twenty-First Century Research Networks." [In eng]. *Eur J Hum Genet* 23, no. 2 (Feb 2015): 141-6. <https://doi.org/10.1038/ejhg.2014.71>. <https://www.ncbi.nlm.nih.gov/pubmed/24801761>.

adulthood should be supported, encouraged, and facilitated.”⁴²

Participation:

Participation in this context “[...] is about individuals and groups of individuals having the right, the means, the space, the opportunity and, where necessary, the support to freely express their views, to be heard and to contribute to decision making on matters affecting them, their views being given due weight in accordance with their age and maturity.”⁴³

Empowerment:

This is the capacitating process aimed at strengthening individuals’ power of understanding and choice and increasing their power and responsibility by improving their skills and knowledge.

Public engagement:

“A common way to describe the public’s awareness and understanding of their participation, in turn, is in terms of their ‘engagement’ with the research... the public can be more or less ‘engaged’ with research whether or not they ‘participate’ in it because engagement is independent of their inclusion as research subjects.”⁴⁴

(Public) Multi-actor engagement:

This is a collaborative, reciprocal, and multi-actor process where all societal actors work together during the whole scientific research process to align its outcomes to the values, needs, and expectations of society.⁴⁵

Capability approach:

This philosophical approach purports that the freedom to achieve well-being is a matter of what people are able to do and to be, and thus the kind of life they are effectively able to lead. It changes the focus from means (the resources people have and the public goods they can access) to ends (what they are able to do and be with those resources and goods). This shift in focus is justified because resources and goods alone do not ensure that people are able to convert them into actual doings and beings.⁴⁶

Citizen science:

This term covers participation in scientific research activities by individuals who are not institutionally bound to the field of science. Participation can mean anything from short-term data collection to

⁴² Larcher, Vic. 2015. "Children Are Not Small Adults: Significance of Biological and Cognitive Development in Medical Practice." In Handbook of the Philosophy of Medicine, edited by Thomas Schramme and Steven Edwards, 1-23. Dordrecht: Springer Netherlands.

⁴³ Recommendation CM/Rec(2012)2 of the Committee of Ministers to member States on the participation of children and young people under the age of 18. Definitions.

⁴⁴ Woolley, J. P., M. L. McGowan, H. J. Teare, V. Coathup, J. R. Fishman, R. A. Settersten, S. Sterckx, J. Kaye, and E. T. Juengst. "Citizen Science or Scientific Citizenship? Disentangling the Uses of Public Engagement Rhetoric in National Research Initiatives." [In eng]. BMC Med Ethics 17, no. 1 (Jun 04 2016): 33. <https://doi.org/10.1186/s12910-016-0117-1>. <https://www.ncbi.nlm.nih.gov/pubmed/27260081>.

⁴⁵ <https://rri-tools.eu/about-rri>

⁴⁶ Sen, A. "Capability and Well-Being." In The Quality of Life, edited by Nussbaum and Sen. Oxford: Clarendon Press, 1993.

intensive use of free time to a high level of expertise.⁴⁷

Responsible Research and Innovation - RRI⁴⁸:

- An approach that anticipates and assesses potential implications and societal expectations with the aim of fostering the design of inclusive and sustainable research and innovation that leads to an acceptable and desirable future;
- and implies that all the societal actors (researchers, citizens, policy makers, business, third sector organisations, etc.) work together during the whole research and innovation process to better align both the process and its outcomes with the values, needs, and expectations of society.

⁴⁷ von Gönner, J. and Herrmann T. and Bruckermann T. et.al. "Citizen Science's Transformative Impact on Science, Citizen Empowerment and Socio-Political Processes." *Socio-Ecological Practice Research* 5 (01 2023). <https://doi.org/10.1007/s42532-022-00136-4>.

⁴⁸ <https://rri-tools.eu/about-rri>

CONCLUDING STATEMENT

It is becoming increasingly clear that biobanks should adopt a forward thinking and strategic approach with regards to biobanking with the next generation by developing frameworks of engagement. This serves to improve trust, thereby making daily biobanking operations more efficient.

Furthermore, it is also apparent that there is the need for a dedicated ELSI role within biobanks, which would aim to support researchers with their daily operations concerning ethical and legal practices. Whilst such a role is often not formally recognised or valued, it does present a significant benefit for biobanks to bring such expertise in-house to respond to the specific needs of researchers and the biobank as well as opening the door to better engagement with diverse publics and thus reflecting the needs, hopes, wishes, and concerns of citizens.

RESOURCES

In addition to the provision of in-house support, it is also advisable to identify external support services offered. This includes services offered by:

- Relevant national regulatory authorities.
- Your National Node.
- BBMRI-ERIC and
- Any other relevant research infrastructures.

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