Ethic and Biobanks

What Are the Steps Needed to Implement Bioethical Issues in a Population-Based and Disease-Based Biobank?

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1 Introduction

In order to answer this burning question,[1] the following sections describe the design and equipment of bioethical issues in a regulatory framework, taking the experience of an Institutional Biobank as a case study. A biobank facility is one of the most valuable means that academic scientific organisations have to improve the competitiveness of their biomedical research, generate research collaborations and develop funding strategies (Zika et al. 2010).

We present the model of a multispecialistic biobank with both a population- and disease-oriented commitment, with the aim of promoting studies finalised at exploiting knowledge on human health and encourage multidisciplinary scientific research. The Biobank will also encourage scientific research basing its activity on an inclusive model of the scientific community in which citizens, researchers, and institutions will actively participate. The analysis of this type of biobank might be useful to cast a light on the issue of bioethics in research activities involving biobanks and foster their role as both institutional and societal infrastructures, as

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well as plots a way forward to implement bioethical issues in a population- and disease-oriented biobank (Jacobs et al. 2018).

A typical multispecialistic research biobank is designed to collect biological samples from both individuals from the general population as well as patients involved in case-control and cohort studies. The facility is structured to house hundreds of thousands of different biological samples, including blood, urine, saliva, tissues, cells and their derivatives. Samples will be preferentially processed in a laboratory pertaining to the biobank and stored in vapour phase liquid nitrogen or in mechanical cryogenic freezers. The software Laboratory Information Management System (LIMS) is designed to support standard biobank operations and thus warrants the traceability of samples and data collection in agreement with the General Data Protection Regulation (EU) 2016/679 (GDPR) guidelines. Operating in a setting that often differs from that of hospital and healthcare facilities, a multispecialistic biobank benefits from having a dedicated consulting room for anthropometric and functional parameter evaluation, sample collection and questionnaire administration.

Biobanks adopt strategies to enhance and maintain the quality of biological samples, from their handling to their final preservation, as well as to ensure data protection. Additionally, working in accordance with the biobanking-specific International Organization for Standardization (ISO) 20387:2019 certification will better guarantee a quality management system with documented standard operating procedures (SOP) and informed consent, in agreement with national and international indications.[2]

We start the analysis of the need to implement the aforementioned biobanking strategies, taking into consideration both the general classification in population and disease-oriented biobanks defined by the pan-European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI), which has outlined two work packages on biobanks entitled WP2 (population-based biobanks) and WP3 (disease-oriented biobanks). At the end of this process, the biobank examined in this study will join the national node of the BBMRI network.[3]

As it is oriented towards disease[4] (Parodi 2015) this biobank will promote research on human disease pathogenesis to improve diagnosis and therapy within specific areas of interest, such as autoimmune disorders and high-impact, chronic age-associated diseases. As it is also population-oriented, this biobank is engaged in

[2] International Organization for Standardization (ISO 2018). *UNI/ISO 20387 Biotechnology – Biobanking – General requirements for biobanking standard*, published in August 2018, specifies the general requirements for the competence, impartiality and consistent operation of biobanks including quality control requirements to ensure biological material and data collections of appropriate quality. https://www.iso.org/standard/67888.html. In Italy, the accreditation of biobanks in accordance with the requirements of this standard will be operated by ACCREDIA.

[3] BBMRI. https://www.bbmri.it.

[4] Disease-oriented biobanks (which may also be referred to as clinical biobanks) are placed at the interface between clinical practice and research. They collect biological samples from patients, and aim to discover and validate genetic and non-genetic risk factors of diseases.

prospective and cross-sectional epidemiological cohort studies involving citizens with specific characteristics or those that are representative of a geographical area, and is designed to address unmet social and scientific needs concerning human health.

To achieve the goal of illustrating a path to implement bioethical issues in a population- and disease-oriented biobank, Sect. 2 will analyse the function of the Data Protection Impact Assessment (DPIA); in Sects. 3 and 4, the *Code of Ethics* and informed consent will be treated as institutional documents. Using the logical themes of broad consent, the research areas and purposes of the biobank will be clearly illustrated in both the regulation and in the informed consent. Section 5 concludes.

2 Data Protection Impact Assessment

The nature of the processing of the data associated with and obtainable from the biobanked samples, from both patients and subjects of the general population, is a significant risk in relation to the rights and freedoms of subjects, particularly certain categories of data being processed, such as genetic data.[5] For this reason, before starting biobank activities and, therefore, the processing, the DPIA is carried out or at least an alternative impact assessment on data protection, as provided by Articles 35 and 36 of the GDPR. Indeed, an assessment represents the mandatory tool for identifying and minimising the risks inherent in samples and associated data processing. In fact, the DPIA is a process designed to describe the processing, assess the necessity and proportionality of processing and to help manage the risks to the rights and freedoms of natural persons resulting from the processing of personal data.[6] The DPIA should be started as early as is practical in the design of the biobank activity, even if some data collection and processing operations are still in progress. Furthermore, updating the DPIA throughout the lifecycle of the biobank will ensure that data protection and privacy are considered and promote the creation of solutions and compliance.

[5] See Garante per la protezione dei dati personali (2019). *Provvedimento recante le prescrizioni relative al trattamento di categorie particolari di dati, ai sensi dell'art. 21, comma 1 del d.lgs. 10 agosto 2018, n. 101*. Roma, Registro provv. n. 146 del 05 giugno 2019. Allegato 1 (4, 5). https://www.garanteprivacy.it.

[6] Data Protection Working Party (2017). *Guidelines on Data Protection Impact Assessment (DPIA) and determining whether processing is 'likely to result in a high risk' for the purposes of Regulation 2016/679* (WP 248 rev.01). Adopted on 4 April 2017. As last revised and adopted on 4 October 2017. https://ec.europa.eu/newsroom/article29/items/611236/en.

3 The Population Biobank Code of Ethics

The need for a *Code of Ethics* emerged from the initial reflection on the mission of this type of biobank, in order to provide an ethical and at the same time regulatory framework for the budding biobank. As known in general terms, the fundamental activities of a biobank[7] are the collection, processing, organised storage and distribution of biological materials and associated personal data for research and diagnosis purposes (Kinkorová 2016). This biobank will be qualified as a 'population biobank', whose prospects and potential are well outlined in the recent Organisation for Economic Co-operation and Development (OECD) document (March, 2021): 'Population-based biobanks monitor the health status of participants over time to assess the natural occurrence and progression of common diseases. These biobanks, combined with genomic and health data, can enable a more personalised approach to medicine by locating the genetic component of human disease. Moreover, [the] growth of genomics markets and associated health sectors offers wider societal benefits including the potential to increase investment in innovation, generate new economic activity and create new jobs'.[8]

Moreover, this biobank is a 'non-profit public institution', a 'service unit',[9] whose mission is characterised by two main purposes: (1) to encourage and increase a network of relations on the territory between bodies and associations dealing with public health, in particular with hospitals and the territorially competent local health services; and (2) to encourage the training of university students, so that they are initiated into rigorous research on a scientific level and respectful of ethical principles.

In the historical time we are currently living in, characterised by the SARS-CoV-2 pandemic, the urgent implementation of territorial medicine has been advocated by many, a future in which population biobanks will play an ever greater role.

The *Code of Ethics* is inspired by the model of 'participatory governance', which, if fully implemented, requires the involvement of all the actors involved: citizens who 'entrust' the biobank with their biological samples and associated data (settlors), and researchers and stakeholders who support the biobank and have expectations of its activities. By adopting this organisational model, the biobank can achieve the virtuous circularity that transforms individual contributions into 'public benefit'.[10]

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[7] The Organisation for Economic Co-operation and Development (2006) defines a *biobank* as 'a collection of biological material and the associated data and information stored in an organized system, for a population or a large subset of a population' (*OECD Creation and Governance of Human Genetic Research Databases. Glossary of Statistical Terms*. http://stats.oecd.org.

[8] Organisation for Economic Co-operation and Development (2021). *Building and sustaining collaborative platforms in genomics and biobanks for health innovation*. March 2021, No. 102, 1. Introduction. https://www.oecd-ilibrary.org.

[9] BBMRI.IT, *Biobanche. Cos'è una biobanca*. https://www.bbmri.it.

[10] UNIUPO (2021). *UPO Biobank*. https://www.uniupo.it/upobiobank.

'Trust' remains the core value in the relationship between a public biobank and settlors, because 'residual biological materials' are transformed by research into important information resources, up to and including the mapping of the biological-informational identity of the person from which they originate. Moreover, it is essential to consider that population surveys might extend to previous pathologies, lifestyles, eating habits and in some cases even to the sexual activity of settlors, whose health is monitored over time. From the widely discussed and now outdated paradigm of 'property rights' on biological materials, the literature has progressed to enhancing the 'personality rights' of privacy. This entails highly complex issues because genomic information is detailed and inherently identifiable in nature. Moreover, this kind of information relates not only to the person from whom it was obtained, but also to their family members.

For all of these reasons, a population biobank must match the 'trust' of citizens with the 'trustworthiness' of its governance: 'It has long been recognised that public trust is crucial if the promises of personalised, genomics-based medicine are to be realised. [. . .] Trustworthiness, the quality of being deserving of trust, is an intrinsic ethical value, and is also instrumental in increasing research participation and improving the perception of research by the public' (OECD 2021, p. 33). Trust and trustworthiness have already gained positive results in clinical trials; 'evidence-based medicine', traditionally linked to 'objective' data, has improved its results by listening to and allowing the active participation of patients and their associations, which today partially fund the research itself (Hamerlijnck 2017; Calvert et al. 2018). Analogous results can be obtained by a biobank which in its supervisory and governance structures integrates[11] the values of the settlors, the expectations of the stakeholders and the needs of a research study to which the clinic proposes challenges of increasing complexity (Winickoff and Winickoff 2003).

In the case of the population biobank, the research ethics review is carried out by the territorially competent Ethics Committee.[12] The Ethics Committee, after having read the Regulations and approved the *Code of Ethics*,[13] plays an active role in the independent review of individual research projects and provides advice on information/consent models. It is a work in progress, fuelled by its awareness that it matures as the activities progress. It is hoped that, at full capacity, the population biobank will have its own 'ethics advisors', whose fundamental task will be to evaluate the impact of the research activities and procedures on the declared ethical principles in order to increase the trustworthiness of the public facility (Cippitani 2019, p. 193).

[11] We consider the model of 'participatory governance' as more appropriate for European regulatory principles, although the 'charitable trust model' or 'biotrust,' proposed by common law jurists, can be taken into account when defining the organisation of a biobank.

[12] European Commission (2010). *European Textbook on Ethics in Research*. Chap. 1. Locating ethics in research, pp. 11 ff. https://ec.europa.eu.

[13] Council of Europe (2006). cit., art. 18.

4 Towards a Model of 'Mixed' (Specific and Broad) Informed Consent

The need for free consent for the purpose of biobanking biological material and related personal data is undisputed. However, a consensus has not been reached regarding the type of consent to be adopted. There is no problem with regard to the 'specific informed consent', which concerns the use of samples and data in the context of a specific and single research study. But this consent does not correspond to the purposes of a biobank, which collects biological materials and personal data especially for future research. A comparison of the logic of 'informed consent' linked to clinical trials allows us to better identify these specificities.

For the purposes of a clinical trial, the logic of 'informed consent' is linked to the therapeutic interventions and the risk/benefit ratio, in terms of efficacy and proportionality of the treatment: the primary objective is treatment, while the processing of personal data is needed by the care relationship. The logic of research on biological samples, on the other hand, is entirely focused on the processing of data which, as highlighted previously, would be able to reveal the biological-informational identity of the person if put through a laboratory analysis. In this circumstance, the benefit to one's individual health is indirect or even remote, while the risks associated with a lack of protection of personal data assume primary importance. These risks can create distrust and lead to a person declining to give their consent or even withdrawing it after it has been given.

For the purposes of the conservation of biological samples, and according to the literature, *broad informed consent* is indicated as appropriate (Hallinan 2020; Mikkelsen et al. 2019). As stated by the Council for International Organizations of Medical Sciences: 'Broad informed consent encompasses the range of future uses in research for which consent is given. Broad informed consent is not blanket consent that would allow future use of bodily material without any restriction. On the contrary, broad informed consent places certain limitations on the future use of bodily materials. Broad informed consent forms should specify: the purpose of the biobank; the conditions and duration of storage; the rules of access to the biobank; the ways in which the donor can contact the biobank custodian and remain informed about future use; the foreseeable uses of the materials, whether limited to an already fully defined study or extending to a number of wholly or partially undefined studies; the intended goal of such use, whether only for basic or applied research, or also for commercial purposes; and the possibility of unsolicited findings and how they will be dealt with. The research ethics committee must ensure that the proposed collections, the storage protocol, and the consent procedure meet these specifications'.[14]

[14] Council for International Organizations of Medical Sciences (2016). *International Ethical Guidelines for Health-related Research Involving Humans*. Guideline 11: Collection, Storage and Use of biological materials and related data, pp. 41 ff. https://cioms.ch.

Similarly, within the GDPR[15] is a direct reference to the broad informed consent in Recital No. 33: "It is often not possible to fully identify the purpose of personal data processing for scientific research purposes at the time of data collection. Therefore, data subjects should be allowed to give their consent to certain areas of scientific research when in keeping with recognised ethical standards for scientific research." This opening was compared with the *Guidelines on consent under Regulation 2016/679*—Article 29 Working Party,[16] in which the 'granularity' of consent is reiterated (§ 3.1.3). This general rule remains valid. But with reference to scientific research, the principle of 'purpose limitation' states that the further processing of personal data already collected for specific purposes "shall, in accordance with Article 89 (1), not be considered to be incompatible with the initial purposes" (GDPR, art. 5, 1 b), provided that the principle of data minimisation is applied, which may include measures of pseudonymisation (GDPR, art. 89, 1).

From this perspective, the Italian Node of BBMRI observes, for instance: "When the purpose can be described only in general terms, BBMRI.it agrees on the fairness [of distinguishing] [. . .] the purpose of [the] research and on the research process, in order to inform [. . .] the area of research in general term[s], but specifically on the process".[17] The fundamental problem for a population biobank is to guarantee the settlors that their data are protected. Consequently, for the purposes of biobanking, the fulfilments of informed consent can be considered respected if the information illustrates the purposes that the biobank pursues, which are 'general' but not 'generic', within which the objectives of individual future research projects are inserted. At the same time, the information must be highly precise and rigorous on the processing of the samples, on the types of analyses that are carried out and on the processing and protection of personal data. From these considerations emerge the intrinsically 'mixed' nature of informed consent for biobanking. It is the responsibility of the competent research ethics committee to approve the individual research projects and monitor compliance with the conditions set out in the international guidelines and applicable legislation.

The 'mixed' model can also be seen as convenient on an operational level. In fact, in current practice, consent is required, starting from specific research, the objectives of which are clearly indicated. Therefore, the information/consent form can be combined or kept separate, with the 'specific' informed consent for the single

[15] 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) (Text with EEA relevance), O.J.4.5.2016 L 119/1.

[16] The European Data Protection Board (EDPB 2020). *Guidelines 05/2020 on consent under Regulation 2016/679*. Version 1.1 adopted on 4 May 2020, § 3.1.3 Granularity. https://edpb.europa.eu.

[17] BBMRI-ERIC (2018). *BBMRI-ERIC joint comments to the Article 29 Working Party Guidelines on Consent under Regulation 2016/679 (wp259) and Transparency under Regulation 2016/679 (wp260)*. January, 2018. National Node - Italy. p. 24. https://www.bbmri-eric.eu/wp-content/uploads/WP29_consent-joint-comments_BBMRI-ERIC_as-submitted.pdf.

research and the 'broad' informed consent with reference to the general purposes of the biobank. However, both consents provide detailed information on the processing of personal data. This simplification is intended to facilitate the request for biobanking by clinicians and the reading of information by the patients interviewed.

The discussion surrounding the consent template acquires meaningful significance and is closely linked to the theme of trust and trustworthiness. In fact, the request for consent to biobanking should not be seen as a final act, but as the beginning of a collaboration path that will last over time. From the perspective of 'participatory governance', we can with good reason speak of an 'interactive and dynamic consent', which also presupposes the use of information technologies, in order to ensure direct and constant interaction between the biobank's settlors, researchers and governance. Information technologies contribute to making settlors feel part of a community that is committed to achieving the objectives of public health, an objective that is sorely needed in the current SARS-CoV-2 pandemic.

5 Conclusion

From the earliest stages of its development, this multispeciality biobank model should be inspired by the indications of BBMRI-ERIC, the European Research Infrastructure for biobanking, in order to better achieve its original institutional goals. As a 'service unit', this biobank aspires to become the vital junction between: (1) the objectives of research in the university sphere, both for the training of young doctors and researchers and for excellence in research, which can offer appreciable results on an international level; (2) support for the translational research of a large hospital-university structure; (3) attention to the health needs of the territory through population studies, particularly on aging, and pathology studies; and (4) the involvement of the population, local government authorities and stakeholders. By progressively involving the population, the biobank will be considered the 'beating heart' of biomedical research in its area. Indeed, as a result of the enduring experience of COVID-19, citizens have understood the importance of research for the protection of collective health.

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