Chapter 10
Public–Private Partnership in Biobanking: The Model of the BBMRI-ERIC Expert Centre

Peter M. Abuja and Kurt Zatloukal

Abstract Biobanks for medical research provide access to human samples and associated data donated by donors or patients. They are typically established and operated by public institutions (e.g., universities, hospitals) and act as trusted partners for the resources, which are considered a common good for the advancement of biomedical research and healthcare. Although the ultimate expectation of donors and patients that their donation will contribute to improving healthcare can only be achieved if profit-oriented industry is able to access their samples and data, there are concerns whenever private companies generate profit based on public resources. In order to overcome this controversy, public–private partnerships, where joint efforts generate value both for the public and private sectors, could be an appealing solution. The BBMRI-ERIC-recognized Expert Centre (EC) is a model for such a partnership. ECs perform analysis of biological samples under highly standardized conditions and in accordance with ethical and legal requirements to generate high-quality data that can be used by industry for product development, and by the public, after a defined period of exclusive use for industry. Thus, expendable biological samples that otherwise could be used only by a small group of researchers are transformed into high-quality data that can be widely shared and used to advance biomedical research and development.

Keywords Biobanking for industry · Public–private partnership · Expert Centre · Trusted partner · Sample and data quality · FAIR data · Open data · Open innovation

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P. Hainaut et al. (eds.), *Biobanking of Human Biospecimens*,
https://doi.org/10.1007/978-3-030-55901-4_10

10.1 Biobanked Human Biological Samples and Associated Data as an Essential Resource for Industrial and Academic Research and for Improving Health Care

Advances in prevention, diagnosis, and therapy of human diseases ultimately rely on the availability of sufficient numbers of high-quality biological samples and data of patients. Biobanks are professional infrastructures for collection, preservation, storage, and providing access to human samples and associated data. They can be established, for example, in the context of specific cohort studies (e.g., large population cohorts) or within the health service [1–4]. Typically, donors or patients provide their samples and data to biobanks as donations, and biobanks are seen as a trusted, publicly funded environment that ensures the proper use of this precious resource for the benefit of certain patient groups or citizens in general. This expectation can only be met if biobanked samples and their associated medical data are efficiently used in high-quality research projects and their results lead to the development of novel products. This translation of a common good (i.e., donated biological samples and associated data) into commercial products, such as new diagnostics or medicines, requires smooth interaction of public and private sectors and transparent models for using public resources for private profit-making industry.

10.2 Major Hurdles for Industry to Work with Human Biological Samples and Data from Biobanks and Possible Solutions

10.2.1 Access to Samples and Data

Biotech and pharma industry need access to human biological samples and data to develop new products. For example, human biological samples are required for the identification of new diagnostic and therapeutic targets, preclinical research, defining disease indications and patient groups for clinical studies, and biomarker or companion diagnostics development [5, 6]. Therefore, providing access to biobanked samples and data is mandatory to meet patients' expectations that their donated samples ultimately contribute to improving healthcare. Nevertheless, the use of donated samples and data by industry to make a profit is viewed critically by the general public (and thus by potential donors) [7, 8]. It has turned out that one of the key factors for patients to donate their samples and data is implicit trust in public research institutions and clinics [9] and that this trust is significantly lower whenever donated samples and data are used in profit-oriented industrial research [10]. Apart from that, human biological samples are per se a costly and irrecoverable resource that should be used in the best possible way, avoiding conflicts of interest or interference with open competition.

10.2.2 Difficulties in Using Publicly Funded Resources for Profit-Oriented Research

Human biological samples and data are very often generated and preserved using public funds (e.g., research projects, healthcare systems, publicly funded biobanks). Releasing samples and data from the public domain for research that is essentially for-profit could therefore lead to a distortion of competition since the same sample cannot be given equally to all competitors that might profit from its use and from the public funding that contributed to its generation and preservation. Even a full cost compensation for accessing human biological samples and data cannot satisfactorily resolve this issue because the boundary between cost recovery (which is allowed in principle) for collecting, processing, storage, and releasing samples and data, and financial gain (which raises public concerns and is not allowed in some countries) cannot be clearly delineated. It is very difficult to correctly attribute the costs of the various processes involved in biobanking to a specific sample and dataset to be used in a project [11, 12]. Furthermore, the generation of biological samples and associated medical data in the context of healthcare involves many persons and institutions (e.g., surgeons, pathologists, oncologists, laboratory medicine personnel, radiologists, biobankers, etc.) who all have a stake in the biobanked samples and data. Therefore, their contribution should also be properly considered in cost recovery, which is not achievable in practice and constitutes, therefore, a potential source of conflicts that may delay or even block some projects. Moreover, the Oviedo Convention on Human Rights and Biomedicine [13] regulates a broad spectrum of issues in research that involves humans. In particular, Article 21 explicitly prohibits financial gain from using parts of the human body. Similar regulations exist in the USA (e.g., the "Common Rule" and the FDA Human Subjects Regulations [14]). On an international level, the UNESCO Universal Declaration on the Human Genome and Human Rights [15] stipulates these issues more generally. The OECD has issued guidelines that focus on the transparency and equality of terms of access to data generated from public funding [16, 17].

To overcome these problems of providing industry access to public biobanks, a model for a public–private partnership has been developed jointly by biobankers, patient advocacy groups, and industry representatives [18]. This model, called "Expert Centre" (EC), is designed to provide a trusted and quality-controlled environment that generates a win-win scenario for both the public and private sectors.

10.3 Public–Private Partnership (PPP) as a Model for Cooperation Between Healthcare, Academic Research, and Industry

10.3.1 What is a PPP?

The meaning of PPPs is somewhat vague since they span a wide range of quite diverse concepts ranging from simple bilateral collaborations to large projects dedicated to generating infrastructures (both physical and organizational) on the European or even global level [19].

In biomedical research and biobanking, PPPs may, for example, aim at developing joint expertise, knowledge, and resources thereby combining the specific assets of the public and the private partners, and so boosting the effectiveness of the innovation process. They come in many variations according to the need they should address [19], ranging from bilateral, small-scale cooperations to large multi-partner, e.g., national or Europe-wide, cooperations. The latter, like the Innovative Medicines Initiative [20], are specifically designed to advance research and development in the biomedical sciences throughout Europe, where the role of the public sector regarding trust and sustainability is emphasized [21].

10.3.2 How can a PPP Work for Biobanks and Industry?

Biobanks are typically established and operated by the public sector. There are however also privately owned and operated biobanks and some big pharma companies operate their own biobanks for their in-house research and development. In this chapter, we focus on public sector biobanks [18, 22].

PPPs in the context of biobanks can complement the large capacities and resources of the notoriously underfunded not-for-profit sector (academic research, public healthcare) with the financial resources of the for-profit-sector (industrial research and development) which would lead to a situation where both sides benefit, provided the legal and ethical issues can be solved. Such a PPP would contribute to sustainable funding of biobanks and provide access to samples/data and transfer of knowledge to private companies. PPPs can also avoid the stigma of selling samples to industry since they can remain in the not-for-profit environment and are transformed into data which are made accessible to the private partner. This enables the generation of data to build a growing public resource that conforms to the FAIR (findable, accessible, interoperable, reusable) principles [23, 24] and is of value both for the private and public partners. Hämäläinen and coworkers have performed a survey of the interaction of European biobanks with industry [22]. They found that most interactions are structured as research collaborations, which resemble PPPs at least to some extent.

10.4 The BBMRI-ERIC Expert Centre Model: A Solution for Many Issues in Biomedical Research

Already during the preparatory phase of the European research infrastructure for Biobanks and BioMolecular resources (BBMRI-ERIC) [25, 26], a PPP (the so-called EC) involving a trusted intermediate was proposed jointly by biobanks, the industry, and patient organizations [7, 18]. The EC performs the analyses of biobanked samples according to the state-of-the art, guarantees privacy and quality, considers pertinent legal and ethical necessities, and, in addition, the sustained public availability of the resulting data according to the FAIR principles [23, 24]. In this context, the EC transforms the biological samples of biobanks into high-quality data that can be jointly used by the private partner and the public.

The concept of the BBMRI-ERIC Expert Centre (EC) model involves:

1. *a not-for-profit public provider of human biological samples and data* that have been donated by patients with the implicit intention of supporting biomedical research. The public partner additionally provides medical knowledge and expertise (e.g., specific expertise of pathologists for selection and preparation of the most relevant tissue samples or clinical oncologists to extract relevant information from medical records) to the EC to optimize the analysis of samples and resulting data. Typically, this is a biobank associated with a healthcare provider and/or medical university or research centre.
2. *a private user of specific data and knowledge*. Typically, this is an industrial partner that pays for the costs of biobanking (not for the samples as such!) and analytical service. The private partner also contributes specific knowledge and expertise (e.g., specific quality requirements or industrial analysis platforms) to the project.
3. *an intermediate EC* that is trusted by both parties and performs the transformation of samples into data. The EC operates on a not-for-profit basis and guarantees to the provider of data and samples that privacy is properly protected and the samples and data are only used according to the informed consent and ethical clearance given. The pre-analytical and analytical workflows are performed according to the latest available standards and under supervision of the industrial partner. In this way, the industrial partner is in control of the quality of the data generated which is a prerequisite for further investments in product development based on these data. The data generated in the EC may be used by the private partner exclusively for a defined period, after which the data must be made available to the public domain.

Figure 10.1 shows the relationships between the key elements of the public and private sectors within an EC.

To make biobanks a resource that can legally, ethically, and technically serve industrial biomedical research and development as a partner, a BBMRI-ERIC-recognized EC must fulfill several requirements. BBMRI-ERIC has issued guidelines for the application to become an EC [BBMRI-ERIC-Associated Expert

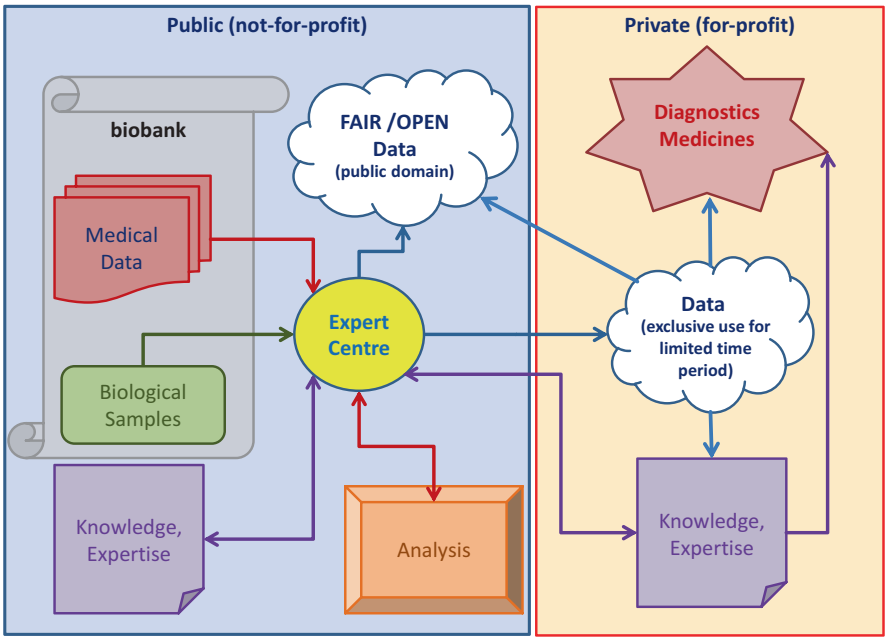

Fig. 10.1 The Expert Centre as a PPP of the public and private sectors

Centres/Trusted Partners, V3.0; www.bbmri-eric.eu] in which the key criteria for ECs are laid down:

1. It must be a trusted environment that guarantees patients' rights to privacy, and at the same time fulfills the donors' intention to contribute to the public good and advancement of medicine. This implies that patients' identities are not disclosed, neither directly nor indirectly. It thus combines the confidential medical and analysis data according to the research requirements and guarantees that this information cannot be used to (re-)identify the donors. Usually, this is done by coding and data aggregation, or by omitting parts of the data that are not required for research (principle of data minimization). The trusted environment, however, in principle retains all coded data, to allow reuse at a later time-point. In this context, special emphasis is placed on the prevention of reidentification of sample donors by combination of data sets from different research projects that use samples and data from the same donors.
2. It performs analyses on the samples in a highly standardized way according to the state-of-the-art thus delivering reliable data to the industrial partner in a transparent way. In this context, ECs pay specific attention to the requirements of a series of ISO standards for the preexamination phase, which are becoming increasingly important so that data generated meet regulatory requirements for future product certification (e.g., certification of in vitro diagnostics according to the European In Vitro Diagnostics and Medical Devices Regulation [27]). A

further requirement is that detailed information on analytical procedures, applied standards, and experimental conditions are made available to the partner since otherwise the data may not be used for product development or cannot be shared later with the public and reused according to FAIR principles. The latter point is actually the reason why the analytical laboratory should reside in the not-for-profit domain: industrial laboratories are certainly capable of performing analyses according to the highest standards however they often do not disclose sufficient meta-information on analysis, standards, and experimental conditions, which is a prerequisite for reuse of data in the public domain.

3. The main value generated by the EC is the transformation of biological samples into high-quality data that can be jointly used by the private and public partners thereby allowing a finite resource to be shared with a broad research community. The interests of the private partner are protected since for the financial contribution a period of exclusive use of the data generated is guaranteed to the private partner. After this period, data will be made available to the public partner to be further shared with the research community. There are several examples of PPPs that have successfully demonstrated how such models of limited data exclusivity work (e.g., Innovative Medicines Initiative).

As of May 2019, three Expert Centers have been appointed by BBMRI-ERIC (Fig. 10.2).

10.4.1 Advantages of the EC Concept

One advantage of this PPP model is that biobanks and ECs can be financially compensated for processing samples into data along the entire patient-to-data workflow and for the maintenance of their biobanking infrastructures without challenging ELSI principles or raising public concerns. The research community (both academic and industrial) can sustainably (re-)use the high-quality data for their own research thereby supporting the motivation of the donors to provide biobanks with human biological samples and data. Another benefit of the EC is that the public sector, in addition to the financial contribution, also benefits from the partnership by receiving expertise and knowledge from the industry partner. Conversely, the private-sector partner benefits from accessing medical and scientific expertise from the public partner (in a much more interactive manner than in typical consultancy relationships). Furthermore, knowledge and expertise, together with assured quality of the data, make the results of this research more reliable and valuable. Last but not least it should provide improved access for private users to public resources.

Sharing of anonymized data instead of samples is becoming a preferred practice, implying that the required analyses are performed according to the highest standards, and only analysis results (not original biological samples) and related metadata are distributed. Medical and analysis data can then be shared in a way that is tailored to the researcher's need while preserving the donors' privacy. This is

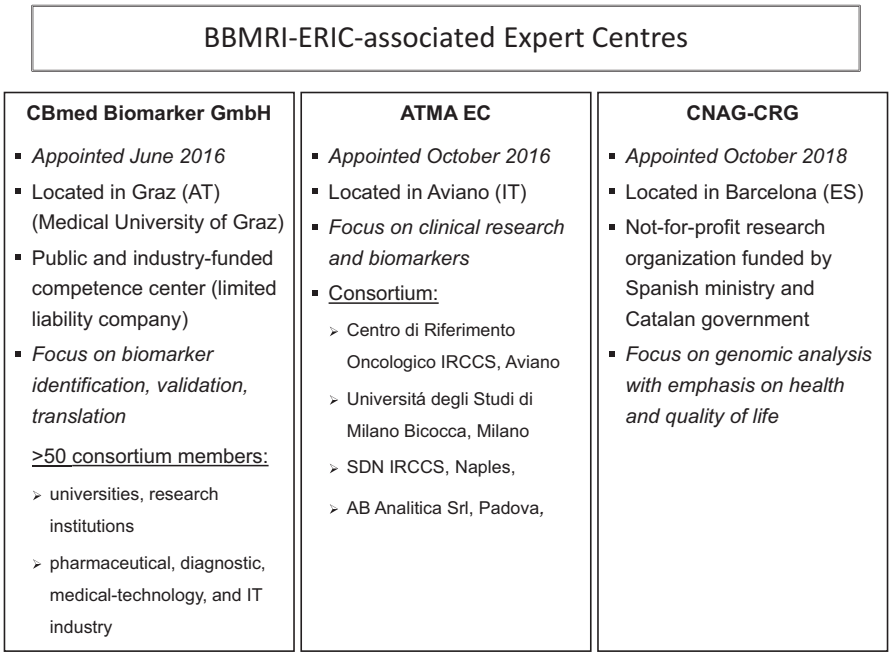

Fig. 10.2 Expert Centers recognized by BBMRI-ERIC (status May 2019)

particularly relevant since the transfer of samples outside the legal domain in which they have been collected may reduce the trust of the donors in the collecting biobank since, for example, using samples for other than the granted use (as specified in the informed consent and approved by research ethics committees) cannot be controlled effectively. Furthermore, most human biological samples contain the donor's genome which can be readily analyzed by next generation sequencing technologies revealing sensitive information such as risk factors of sample donors and their relatives and potentially allowing linking and reidentification of data. Another aspect is that there are several countries that have legal restrictions for sending biological samples to other countries for analysis. In this context, ECs could be a good solution for integrated sample analysis in international research collaboration since the need for sample shipment is avoided.

10.4.2 Sample and Data Quality

To ensure reliability and interoperability of analytical data, academic and industrial biomedical research requires access to high-quality human biological samples. The importance of sample and data quality is underlined by the "credibility crisis" in biomedical research that has disconcerted the scientific community [28, 29].

Furthermore, diagnostic errors contribute to 10% of patient deaths, and more than 50% of errors in laboratory tests can be attributed to pre-analytical factors, i.e., sample quality [30, 31]). Analytical performance gained further relevance in the context of personalized medicine, where most new drugs require a companion diagnostic test in order to select the right patients to treat [6]. In this context, the performance of a diagnostic test relates to the performance of very expensive drugs. These and other factors led to the series of ISO standards for the preexamination process and to new regulatory requirements such as the European Regulation (EU) 2017/746 on in vitro diagnostic medical devices [27].

Major efforts have been made in the last decade to introduce standards for sample quality, both for research and diagnostic applications, covering the whole pre-analytical workflow from sample collection to transport, processing, storage, retrieval, and isolation of various analytes (e.g., through the projects SPIDIA and SPIDIA4P [www.spidia.eu]). Previously, the importance of verification, standardization, and documentation of pre-analytical processes was insufficiently recognized, also because the focus was on optimization and standardization of the analytical technology itself. Meanwhile, standardization of the whole patient-to-data workflow has turned out to be of crucial importance and has a large impact on the data quality that industry (and also academia) requires. Therefore, ECs place much emphasis on sample and data quality, and processes have to meet the requirements of international standards. In order to demonstrate compliance with standards, proper quality management systems have to be in place. This may include certification or accreditation of ECs according to the relevant norms.

10.5 How Public–Private Partnership Models can Stimulate Innovation

10.5.1 Open Innovation, Biobanks, and Expert Centres

As PPPs, ECs implicitly foster collaborative research in the sense of Open Innovation by generating Open Data. This is due to the condition under which ECs operate, namely that the high-quality data they produce should be made available to the public domain following the FAIR principles, considering also the specific requirements of health-related FAIR data [23, 24]. In this context, it is important to emphasize that Open Data may not undermine ethical and legal requirements and specific access procedures for their use have to be applied. Since industrial partners support the sample-to-data conversion by paying for the sample analysis, they may also negotiate a period of exclusive use of the data generated within the EC. It is, however, desirable that this period is not too long. Similar provisions apply, of course, also for the academic exploitation of such data, e.g., for publications. Open Science benefits from EC-like PPPs since the publicly available data can serve further studies and minimize the need for reanalysis of original biological samples. This not

only increases the use of the finite original biological samples but also avoids duplication of analysis efforts and finally speeds up the innovation process because research can build on existing data. At the same time, research based on Open Data is often more competitive since several groups may access the same data set and the intellectual property (IP) developed on the basis of Open Data has to be protected as soon as possible.

10.5.2 Management of Intellectual Property (IP)

Protection of IP is a prerequisite for the industry to invest in product development. Therefore, it is imperative for ECs to provide opportunities for the private partner to protect IP that emerges from data generated in the PPP. Protection of IP (which is not opposed to Open Data and Open Innovation [32, 33]) may require a grace period before data are made accessible to the public during which IP can be protected and, at least to some extent, a product developed and the market secured. Securing IP for an invention resulting from data generated in an EC that later becomes Open Data is not problematic since the openness relates to the data, not to the invention derived from them. However, subsequent controlled revealing of data and details (in the form of published patents, scientific publications, publicly available technical specifications) can lead to the generation of complementary assets (in the context of Open Innovation) as well as competing products.

There might also be situations in which EC-derived data per se do not lead to IP and therefore could be released immediately without compromising the innovative advantage of the private partner.

10.6 Conclusion

PPPs provide an environment for public biobanks that facilitates access to samples and data for industry and avoids concerns and legal barriers for using publicly funded resource for profit generation in private companies. BBMRI-ERIC-associated ECs are a specific type of PPP, which generate high-quality data as a common benefit for the public and private partners. In this context, it is critical that ELSI issues, particularly the protection of privacy of the sample donor/patient, are guaranteed and that biosamples and analytical technologies are of the highest quality. This is a prerequisite for the industry to use the data for further product development, and for the data to be widely reused (after a limited period of exclusive use for the private partner who has funded the analysis) by the scientific community. Insofar, ECs may become a prototype for FAIR and Open Data producers thereby stimulating Open Innovation.

Acknowledgments This work has received funding from the Horizon 2020 Research and Innovation Programme of the European Union, projects ADOPT BBMRI-ERIC (Grant Agreement No. 676550), CORBEL (Grant Agreement No. 654248), and the Austrian Federal Ministry of Education, Science and Research, project BBMRI.at [GZ 10.470/0016-II/3/2013]. We thank Dr. Penelope Kungl for critically reading the manuscript.

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