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Networked research infrastructures and their governance: The case of biobanking

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Research infrastructures such as biobanks are increasingly important for science and society. This paper focuses on the transition of biobanks from being a research tool of individual research groups to complex, internationally networked research infrastructures supporting large-scale biomedical investigations, and the challenges that this change poses for governance in relation to management, funding, ethical and legal issues. A major problem for most publicly funded biobanks is that funding remains time-limited and is normally associated with specific research projects. Yet, as biobanks are becoming large research infrastructures, they are requiring new forms of sustainable funding. Based on ten in-depth case studies with biobanks of different sizes from different EU countries, we conclude that the growth in scale triggers the need for different governance structures, based on the specialization and professionalization of technical tasks, the formalization of many management practices and a shift in funding structures.

Keywords: biobanks; research infrastructures; networking; governance.

1. Biobanks as research infrastructure

Research infrastructures are crucial for scientific research and are an important element of science policy. Because of their high and growing costs, they have become the object of international collaboration, and have attracted the attention of policy-makers and scholars. The value that these facilities could generate has been the subject of many studies and impact assessments (Juhlin et al. 2009; Zuijdam et al. 2011). Work has focused on the different ways in which research infrastructures can create socio-economic value, it has identified commercial products and services based on the results of research using such infrastructures, and has identified spill-over effects triggered by the leading-edge technology needed to build and operate them (Bureau of Industry Economics 1992; Hallonsten et al. 2004; CERN 2005; Groenewegen and Wouters 2004).

However, the governance challenges posed by these research facilities have not attracted similar attention and policy-makers and research-funding institutions often remain unaware of the difficulties likely to be encountered as the infrastructures grow and develop. Research infrastructures pose governance challenges related to their legal status, the avenues for coordinating the supply and demand of research services, and their management as a research service. From a legal point of view, they are complex, with some having the status of a university department, others being agencies, and still others operating as research institutes (Porcheray and Lavocat 2008). The alignment between the supply of research infrastructure services and societal needs has also proved problematic.

For example, it has been noted that in nanotechnology, there is a lack of coordination between R&D infrastructures, researchers working in different disciplines, and the areas of application where these research resources might be used (Malsch 1997). Finally, they are often impaired by casual approaches to management. For instance, many European research infrastructures are unable to provide general data on users (Porcheray and Lavocat 2008).

Much effort has been invested in the analysis of large centralized research facilities (OECD 1995), but new types of organization are emerging that pose specific problems. Our interest here is in networked research infrastructures. A networked research infrastructure is a facility based on geographically distributed facilities, instruments or datasets (e.g. including collections of biological specimens). Although the individual facilities that constitute the networked infrastructure may be small, they operate in coordination with other facilities which in combination create a large infrastructure. The aim of this paper is to analyse the governance challenge posed by biobanks, a specific group of infrastructures that have been evolving towards a networked architecture. Biobanks are crucial for the development, among other subjects, of biomedicine. Until recently, the growth of biobanks has been driven mainly by 'bottom up' initiatives with some regional and national networks bringing together existing facilities. Increasingly, new initiatives are starting to create networks based on a more directed, 'top down' approach. This means that, rather than the network being the result of an initiative bringing together existing small biobanks, it is the outcome of a large project creating a distributed set of biobanks with a central organization and management structure. In both cases, coordination is difficult, particularly when the facilities are distributed across countries with different regulatory and research management practices.

This paper addresses the evolution of biobanking from dispersed, small facilities to a set of large networked infrastructures and large biobanks, and analyses the new governance and funding challenges that this change has triggered, along with the policy responses required to address them.

2. Changing role of biobanks in research

Biobanks collect, store and distribute biological materials and their associated data (e.g. health information, physical measures, life habits, socio-demographic and socio-economic characteristics). They are sample repositories and provide related services to researchers. Our focus is on biobanks collecting human biospecimens to support health research. In this context, biobanks operate as an interface between sample (e.g. tissue, blood, DNA) donors and biomedical researchers, in an academic or pharmaceutical setting. Thus, biobanks must remain committed to donors' rights (e.g. informed consent, protection of personal data) while serving the needs of researchers. In general, biobanks are expected to improve our understanding of the interactions among genes, the environment, lifestyles and diseases, and then to help translate this knowledge into clinical practice through innovative diagnostics, therapeutics and preventive treatment strategies. More specifically, samples can be used to identify and validate drug targets, identify disease mechanisms, and develop and test new drugs based on biomarkers.

The number of biobanks has grown rapidly over the last decade. There are currently more than 400 biobanks in Europe, which hold hundreds of thousands of samples (Editorial, 2009). These biobanks are very diverse and exist within a variety of organizational settings such as: medical research institutes, or pharmaceutical and biotechnology companies, or as standalone organizations. They differ in size, operational practices (how they access samples and relate to researchers and other biobanks), geographical scope and funding mechanisms. According to Tutton (2007) there are at least three main types of biobanking activities:

- Population-based prospective biobanks aimed at studying the development of common, complex diseases over time. The first such initiative was deCODE Genetics, a private venture capital funded company based in Iceland (Chadwick 1999). Other population-based biobanks can be found in the UK, Estonia, Norway, Singapore, Tonga, Latvia, Japan and Gambia.
- Collections of tissue samples and clinical data on specific diseases and non-diseased controls, targeting the development of treatments for the specific diseases. These biobanks are often involved in the discovery or validation of genetic and non-genetic risk factors. They include collections of tissue samples and clinical data held by pharmaceutical companies and clinical research organizations from clinical trial subjects.
- Organ biobanks and other sub-population biorepositories (twins etc.) assembled by different groups working on the same problem in order to increase the statistical significance of the samples, for example, for the study of rare diseases or differences between genetic and lifestyle factors.

The size of these biobanks in terms of the number of samples they store, ranges from several hundreds to millions. During the last decade, however, the size of biobanks has been growing. One reason for this growth is the rapid progress in genomic approaches to biomedical research moving from the study of rare monogenic diseases to common, multi-factorial diseases (Collins et al. 2003). Researchers are demanding larger biological datasets in the expectation that high-throughput technologies will enable better dissection of complex, causally heterogeneous diseases into more specific diagnostic entities (Hoheisel 2006; Burton et al. 2009), and that the resulting biology-based definition of disease categories will enhance

the development of more effective treatments, reduce undesired side effects of new treatments, improve success in clinical trial design, and lead to new concepts in disease prevention.[1] Despite these high expectations, however, biobanks still face a range of operational and methodological challenges (Tutton 2007).

3. Our approach

The data for this paper are derived from a study carried out for the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) (Meijer et al. 2010). The BBMRI is funded by the European Commission Framework Programme (FP7) to develop a virtual research infrastructure; it involves more than 260 biobanks and research institutions in 30 countries. Its central goal is the creation of a sustainable infrastructure organized as a 'federated network' of European biobanks.[2]

This study used a variety of methodologies, but in this paper we draw on two specific sets of evidence:

- Information about the evolution of the BBMRI initiative. This was drawn from direct participation in BBMRI internal meetings[3] and open conferences,[4] and from official BBMRI documents. The internal BBMRI meetings provided the opportunity for participatory action research and the open conferences were used to carry out interviews with a broad set of participants. We consulted official documents for information on the network's goals (both explicit and implicit), its evolution and the challenges it faces in the pursuit of its goals.
- Information about the evolution of specific biobanks. This was analysed through ten in-depth case studies (see Table 1). The ten biobanks were selected according to seven criteria: age of biobank, country of origin, number of samples, types of samples, host institution, organizational form, and funding. The cases are geographically spread over Europe and both virtual networks and 'physical' infrastructures are included. Two of the biobanks were non-BBMRI members, which decreases the possible biases when drawing conclusions on BBMRI-related issues. We used semi-structured interviews with biobank directors, coordinators, researchers, technicians and, when relevant, user organizations. The interviews were transcribed and each biobank was given the opportunity to comment on the text prior to its analysis. Interview results were complemented by documentary research. The case studies provide a fine-grained analysis of the way different types of biobank have evolved and structured their collaborative strategies.

4. Evolution of biobanking

4.1 Towards larger or networked collections

Despite the diversity of biobanks, their evolution follows some clear patterns. The origins of many biobanks lie in individual or small groups of researchers building repositories to respond to their own research needs. The case studies revealed that pre-2000 the concept of biobanking, as a specialized infrastructure providing services to researchers, was not widespread.

In the first decade of the present century, biobanking took off as an identifiable concept, driven by the trend towards ever larger collections which developed for two main reasons. First, as already argued, researchers wanted access to larger collections, mainly because of the need for greater statistical power to address genetic and environmental factors in multi-factorial diseases. Second, there is an economic logic driving the formation of larger or networked collections: research funders can benefit from more effective investments by distributing the fixed costs of managing and maintaining collections across larger sample-sets.

Table 1. Ten case studies

Case	Year started	Country and coverage	Organisation	Funding
DeCODE	1996	Iceland (national)	C	Private (75%) + public (uni)
Estonian biobank EGPUT	2001	Estonia (national)	C	Public (uni + gov) + private + EC
UK DNA Banking Network	2003	UK (national)	M	Public (gov + uni + grant)
ENGAGE	2008	International	D	Public (EC + uni)
TransBIG	2007	International	C	Public (EC + uni)
Tumor Bank Castilly y Leon	2004	Spain (regional)	C	Public (gov reg + central)
Telethon	2008	Italy (national)	D	Charity + public (uni)
EuroBioBank	2001	International	D	Public (EC + charity)
Huddinge Brain Biobank	1976	Sweden (national)	C	Public (uni)
Biobank Medical University Graz	1993	Austria, Hungary	C	Public (gov + uni + EC)

C = centralised, D = decentralised, M = mixed, EC = European Commission, uni = university, gov = government, reg = regional

The short history of biobanking is therefore an account of the creation and management of larger (biological) datasets. The initial steps towards building biobanks were based on previous experience of sample storage and management, as for example, in the case of Telethon and the Biobank Medical University Graz. These initiatives brought together collections that had typically been attached to specific research groups or projects and had been built and managed as part of the research work of the researchers involved. The scope of the first biobanking activity, as a distinct activity that separated the generation and management of the samples from the actual research, was limited in its geographical scope, in relation to the origin of the samples and the location of itspotential users. In our sample, seven out of ten cases were initially nationally- or regionally-based, but all evolved towards offering larger datasets, to increasingly dispersed research teams, either by merging to form larger more centralized repositories or through networking existing facilities to address study areas such as cancer, rare diseases, and common complex diseases. In this initial stage, many of the new biobanks were already international, and international collaboration often extended even beyond cooperation among EU member states, as for example, the case of ENGAGE. Biobanks fuel research, but have evolved to become separate organizations from research groups.

The actors leading this process vary from country to country. It is led by patient-driven organizations in Italy, research institutes in France, and government funding organizations in Spain. In other European countries, consolidation is being achieved through specific national networking initiatives, such as in the Netherlands, where government has funded a BBMRI-NL, and in Sweden through the BBMRI.se. Despite the variety of actors involved in leading this process, developing large collections poses interrelated organizational, management, governance, funding, and outreach challenges. The rest of this section analyses these challenges.

4.2 Organizational forms

The variability of organizational forms can be exemplified by referring to two main features: the physical location of samples, and the establishment of managerial control over collections. Fully centralized facilities have a single location for the samples and a unified management structure physically located at the same site. However, not all sample locations and management structures are aligned in this way. Some biobanks that describe themselves as having a central location have samples stored at different sites managed from a single central site. One example is the EuroBioBank, which has a central management structure, but has samples stored with collaborating national biobanks. The reverse also occurs: in the case of TransBIG, for instance, a dispersed group of researchers decided to store 'their' samples in a centralized location, but to retain control over their respective collections. A central sample repository does not necessarily imply a unified management structure. Mixed situations can occur: UDBN stores samples in a central location, but the collector, who is located at a university, retains some samples onsite.

Organizational structure has consequences for arrangements over access and governance. The variability of organizational forms complicates the development of management and governance approaches: learning from each other is limited by the different organizational settings, and 'best practice' can be defined only in relation to specific types of biobanks.

4.3 Management

The increased number of samples required for research cannot be satisfied simply by scaling up biobank operations. Offering services to growing numbers of external researchers poses new problems that require specific managerial approaches. A large repository, or network of repositories, managed centrally, will require closer monitoring of operations, of numbers of samples being distributed to researchers, and the results of their research. Our case studies show that biobanks that were set up to provide services to a wide research community (such as UDBN, Telethon, EuroBioBank and the Estonia Biobank) monitor external access to samples: they keep track of the numbers of samples distributed, and of applications for samples. Further, biobanks managed by patient associations consider such monitoring to be important for accountability. Likewise, some research funders require specific monitoring practices.

Large biobanks, operating as a service to researchers, differ from their smaller researcher-managed predecessors in several other respects. They are becoming professionalized: that is, many of the tasks that researchers carried out in small and localized biobanks have become the functions of specialist personnel. Such tasks include: the development and implementation of quality systems for handling samples, catalogues, and equipment, and the development of formal processes to train and certify the specialized technicians needed to run the facility.

The emergence of formal quality assurance systems is particularly important for sharing information between biobanks. When the researchers were in charge of managing 'their' samples they were in direct control and could satisfy themselves that the samples they were exploiting were handled properly. When sample handling becomes separated, crucial parts of the research process are left to third parties, and researchers feel the need for assurances that these processes, over which they have no control, have been carried out correctly. Also the compatibility of samples, data formats and standard operating procedures needs to be assured before samples can be compared, merged or connected. Formal quality assurance

processes satisfy this demand. According to BBMRI, 43 member biobanks have adopted quality management processes that adhere to ISO9000 or ISO9001, and 30 have generated specific norms based on national standards and OECD regulations. However, the variety of quality assurance standards poses new problems. Biobanks using different norms may be reluctant to share samples and coordinate operations unless they formally recognize each other's quality processes or agree on the same procedures. Such standardization and harmonization procedures are costly and call for extensive documentation of internal sample handling and management procedures and external, independent certification of the procedures. Thus, the evolution towards larger biobanks has generated bureaucratization of this important part of the research process: standard rules and procedures have been put in place and a management structure has been developed to ensure that the rules are followed.

Our case studies provide evidence of trends towards tighter coordination of biobanking operations, which, as already discussed, represent a very varied range of initial conditions. In addition to the formalization and harmonization of sample handling processes, tighter coordination is being achieved through the implementation of information and communication technology tools enabling database access and search. The actors leading this coordination and harmonization vary from country to country. In Italy important early initiatives were driven by a charity. In Spain the drive for coordination has come from central government. In other countries, European projects have been the main driver of increased coordination.

4.4 Legal and social issues

Governance issues in biobanking typically refer to the way that ethical, legal, and social issues (ELSI) are addressed. Here, the evolution of challenges and the types of solutions emerging parallel those discussed in Section 4.3. Concern about ethical issues, regulatory and legal approaches across different countries began to play a role as biobanks developed (Hirtzlin et al. 2003). Similar to management and sample handling practices, harmonization of ethical considerations and legal approaches is important when samples are exchanged and used beyond the physical boundaries of the biobank. Ethical, regulatory and legal issues are particularly problematic when operations become international. National regulations on issues such as privacy, data protection and ethical frameworks vary significantly across countries. Differences in legal systems, even when apparently small, can emerge as insurmountable barriers to the distribution of samples across borders (Hansson 2011; Yuille et al. 2010). Even if EC directives exist, these can be interpreted differently across countries (Zika et al. 2008).

To enable international networking and integration of samples and data, there is a need for international harmonization in areas such as: quality control systems, consent, confidentiality, data ownership and intellectual property policies (Gottweis 2005; Gottweis and Zatloukal 2007). Harmonization and coordination at the legal level poses different challenges to those presented by ethical issues. Legal issues are codified, and, although complex, can be addressed through specific technical tools. BBMRI, for instance, has pioneered an interactive approach to address the legal issues associated with pan-European biobanking through the establishment of a wiki legal platform.[5] The wiki is used to share, discuss, validate and issue authoritative and reliable legal forms and templates. Ethical questions, however, are more difficult since their definition and meaning may be contentious. BBMRI, for instance, has devoted substantial effort to tackling ethical issues and concludes that the term 'harmonization', in this context, should be regarded as the establishment of common standards, but that this is not sufficient. Agreement on the ethical credentials of any international biobanking initiative is a prerequisite (Chadwick and Strange 2009). Harmonization is thus an 'ongoing process' rather than an endpoint. The establishment of standards allows for the exchange and interplay of different views including 'voices less often heard' (Cambon Thomsen n.d.; Johnsson et al. 2008; Laurie 2008).

There is a cost in terms of time and resources for addressing these issues. The effort will be more intense for international initiatives, which will have to deal with different ethical cultures, legal restraints and *de facto* practices.

4.5 Funding

The move to larger biobanks calls for different funding structures. Biobank funding covers a diverse set of activities: sample collection, set up, maintenance, research costs and outreach activities. Importantly, the need to tackle ELSI harmonization and to specialize and professionalize many of the tasks associated with the running of a biobank, implies a substantial increase in the proportion of overhead costs over direct running expenses. The financial structure of a large biobank or networked infrastructure is very different from that of a small biobank oriented to satisfying the research needs of an 'internal' team of scientists. The study of biobanking in six European countries in the early 2000s by Hirtzlin et al. (2003), found that banks were usually funded from the host institution's budget. This evidence is supported by the findings in our study that traditionally small biobanks were funded by a combination of public and private sources. The most frequent division is for personnel and maintenance costs to be covered by the institution, and research expenses to be met by grants from public sources such as EU, national and regional agencies. The problem is that funding from research projects is limited, in terms of both volume and time.

The need to move towards a different financial structure may explain why, despite pressure to shift to large biobanks operating as research infrastructures, the majority of biobanks analysed in our case studies remain 'internally oriented' notwithstanding their increasing size. The costs of sample collection for a new biobank are in the range €4–8 million, depending on the number of samples. When the set up of a biobank involves a new building, the costs are even higher. Once a biobank is established, BBMRI estimates that the average annual operational cost is €500,000 (range €400,000–900,000), of which 50% is for personnel. These high expenditures are increasing calls for studies to ascertain the costs of operating specific biobanks. However, there is very little detailed information available on the actual costs of setting up and operating a biobank, a problem that can be traced back to the initial stages of biobank development. Through our case studies we found that the majority of biobanks allow only limited access to external users and only on an *ad hoc*, informal basis, typically free of charge. According to BBMRI, less than 10% of member biobanks implement some sort of cost-recovery scheme. In line with this estimate, only one of the biobanks in our case study (i.e. UDBN) charged to cover administrative costs or the marginal costs involved in providing samples.

This situation is not sustainable in the long run. The larger biobanks require more expensive physical infrastructures that are unlikely to be sustainable by single research groups. Also, the need to operate as a service provider to a European or even global community of researchers in order to distribute the costs of the physical infrastructure among a larger base of researchers, has the effect of increasing, even further, the fixed costs necessary to run the facility. As we have already argued, the fixed costs will have to raise to cover the overheads associated with the implementation of quality procedures and the professional specialists required to run different aspects of the operation. As biobanks grow in size and mature into a research infrastructure, their cost structure is becoming more complex and requires stable, long-term funding sources and a funding model that does not centre on a small number of specific short-term research grants. Potential ways to raise funds include: charging user fees, selling data services, and collecting royalties on intellectual property developed using biobank resources (International Data Corporation 2004). However, generating a flow of commercial resources is unlikely to cover all the costs of running a biobank,[6] as demonstrated by the bankruptcy of DeCODE. Additional stable sources of core funding will be necessary in most cases, from the public sector, patient organizations and private foundations. Developing these sources of income will require a proactive approach from biobank managers and development of outreach activities.

4.6 Outreach

For biobanks to move along the development path identified here, will require a different funding structure. To be able to develop sustainable funding patterns and to encourage pools of volunteers to provide samples, will, in turn, require outreach activities. By outreach we mean the range of activities designed to communicate the activities of the biobanks to specific communities and to engage their support. We can distinguish three main types of outreach that would help to develop a research infrastructure:

- To the scientific community: The main way to raise awareness and visibility of the biobank as a potential resource for external researchers is through scientific papers. In this context the main problem biobanks face is that there is neither an established procedure nor a common practice to acknowledge the contributions that biobanks have made to the development of the research.[7]
- To industry: Many biobanks do not consider the direct involvement of industry in their activities to be a priority, as a client for their services or as a collaborator to develop a common infrastructure. Although collaboration with industry could be a major source of funding it is difficult in practice to provide access to industry because of conflicting interests. Commercialization of human biological samples is prohibited by the European Oviedo Convention ETS164 and the national legislation of many countries. Although cost recovery is legally allowed it is not generally accepted by donors and patient organizations since they want donations of biological samples to be placed in the public domain. This is often at odds with industry interests. Industry generally wants samples to be private because they confer competitive advantage. Our interviews show that industry is interested in accessing the type of large-scale data that can be provided by a large biobank. One way to circumvent the legal issues associated with public–private partnerships is to only provide aggregated data, not individual information. To an extent, this has been addressed by the concept of expert centres. These public–private partnerships carry out pre-competitive research whose results are openly made available to industry. At the same time outreach activities are not only a one-way communication channel from academia, but they also enable academics to learn from industry. Big pharmaceutical companies have, for instance, experience in the type of legal, ethical and technical issues that the international networking of biobanks raises.
- To society: Outreach to society will focus either on specific groups, such as patient organizations, or the general public. The objectives are multiple, from general awareness, to recruitment of donors. A number of issues need to be considered when addressing the broader society, as was

suggested by the Eurobarometer survey (European Commission 2010) conducted in 2010. The results show that, although people in most countries were not worried by the prospect of providing samples and lifestyle data, access to medical records and genetic profiles was regarded with concern by 12 and 10 countries, respectively. This preliminary analysis underlines the importance of trust, the preference for narrow consent in general, and the preoccupation frequently encountered over privacy and data protection.

As the complexity and costs of biobanks increase, outreach will be necessary to increase their visibility and to acquire political, financial and operational support (Gottweis et al. 2011). Large biobanks will require substantial economic resources, access to large numbers of individuals to build their collections and, in certain areas such as rare diseases, good social awareness. Higher visibility is important when substantial long-term public funding is sought. Thus, biobanks are in direct competition with other large scientific infrastructures for public investment (Gaskell and Gottweis 2011). Yet, the case studies show that outreach activity remains very limited. Biobank managers seldom consider outreach a priority and the activities that are implemented are typically limited in scope. Currently, most biobanks do not have a formal outreach strategy, the exception being patient-led biobanks which have greater links with the communities they serve (EPPOSI 2006). To be able to engage with the external community the introduction of new priorities and the acquisition of new skills will be needed. Given the general public's limited knowledge and the complexity of the issues at stake, a well thought out outreach strategy should be part of a professional organization.

5. A system in transition

As professional international research infrastructures for big science, biobanks can play a central role in an increasingly complex research environment and are required to develop accountable and transparent management procedures. Driven by scientific and economic factors, biobanking is in a process of transition from individual research tools to complex international research infrastructures. This process is not an ordered and homogeneous change, but rather a complex and problematic transition. First, biobanks are evolving along different paths, according to the context in which they operate (Mayrhofer 2010). For instance, UK UDBN's deployment of cost-recovery procedures and sample distribution tracking can be attributed, in part, to the importance of project-based funding in the UK research system. UDBN draws substantial funding from a variety of projects and this calls for more rigorous accountability. In Spain, the importance of regional governments in the management and funding of the health and research systems has led to the development of regionally-based networks; there is therefore a higher level of fragmentation than in other countries.

Another factor explaining the diversity of biobanks is that large-scale population-based biobanks are a relatively new activity. Although seldom recognized as an independent activity before 2000, many new initiatives have emerged over the last decade. As new biobanks are launched, these initially are adapted to their specific local conditions and research objectives. A variety of organizational forms is emerging as a consequence of the diversity of the contexts in which they operate. However, we identified some general trends and challenges that are pushing biobanks towards increasingly convergent development paths.

As biobank infrastructures grow in size and complexity they need to pursue new types of activities such as: a focus on societal outreach, a change in funding structure in favour of long-term sustainable sources, the establishment of international standardization and harmonization methods including the adoption of formal systems of quality management and control, and the development of new legal entities to manage the emerging networked international infrastructure.

As already discussed, these changes are not easy to implement. Although several EU countries are dedicating funding streams to foster the integration of their national facilities into pan-European infrastructures, the dominant funding mechanisms continue to be linked to specific research projects. Specific projects seldom secure funding for periods of longer than five years, but like most research infrastructures, biobanks have a much longer operational life. Further, funding strategies need to evolve as the biobank progresses through its different stages. Initially, the setting up of a biobank can take about two years, and its costs may be covered by specific grants. Yet it is also difficult to make further funding conditional on the achievement of certain performance objectives. In biobanking, as in other research infrastructures, the initial funding period will be devoted exclusively to setting up the facility. Specific targeted funding is typically used to finance the start-up phase. Once the biobank is working it generates substantial operational costs, including personnel to maintain the samples and the equipment, operate the IT systems, manage the infrastructure and equipment, implement the ELSI procedures, and engage in networking and outreach activities. The costs that need to be covered are usually too high for one institution or even one country to bear. Typically, many biobanks fund their operations through extracting a share of the funds received by the projects that use the facility. In practice, an infrastructure is funded as if it was a set of projects. Funding is obtained through traditional national and international research grants, including the EC Framework Programmes. There is a need, instead, for a mixed method of funding, combining a core long-term infrastructural funding (like the funding that national governments, charities and other

organizations already offer in same cases) with other forms of funding such as cost recovery, public–private collaboration, and short-term projects, requiring new business models.

This paper shows that the evolution of these research infrastructures is contingent not only on securing funding sources, but also calls for a complex set of organizational, managerial and governance changes. If biobanks are able to adapt to the new circumstances by adopting new organizational and governance forms, we are likely to witness a reduction in their diversity: larger organizations with international scope will be formed on the back of a professionalized specialization of tasks, a more bureaucratized managerial structure including a complex set of standardized managerial procedures and ethical approaches, and more monitoring and evaluation of results. This is a challenging set of requirements: public support of biobanks cannot be constructed on the basis of funding alone, but also needs to take account of the organizational and governance issues addressed in this paper. If national and EC policy wants these large research infrastructures to be successful, it must be aware of and contribute to these changing governance and funding requirements.

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Notes

1. Analysis of complex diseases is difficult because they are caused by a large number of small, often additive effects. Revealing these complex interactions depends critically on the study of large sets of well-documented, up-to-date epidemiological, clinical, biological and molecular information, and corresponding material from large numbers of patients and healthy people, collected and made available by biobanks (Hagen and Carlstedt-Duke 2004; Manolio et al. 2006).
2. For more information regarding BBMRI see <www.bbmri.eu> accessed 31 Aug 2011.
3. Internal BBMRI member meetings held March, June, September and November 2009.
4. Joint (public) meetings of BBMRI participants and associated members March and December 2009.
5. See <http://www.legalpathways.eu/> accessed 17 Dec 2011
6. So far, the biobanks in our case studies have been funded from private and public sources. Personnel and maintenance costs usually are covered by the institution hosting the biobank, and the additional costs of processing samples and data, because they are linked to research projects, are funded by research grants.
7. The Italian Telethon biobank is working with ISI Thomson to assess its contribution to science through citation impact analysis, but such efforts are rare.

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