Biobanking in Cancer Research

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Introduction

The availability of a biological resource such as human tissue and its derivatives for research that is fit for purpose and linked to well-annotated clinical data under approved ethical protocols is an essential facility for biomedical research, especially in the present era of personalized, translational medicine. The importance of these facilities have been recognized in the popular media with Time Magazine (2009) identifying biobanks as one of the ten tools of significance in recent times that have contributed to health and well-being [1]. Recent investments to upgrade the health department's databases held by government and institutional registries, with electronic data mining and linkage tools, now means it is possible to perform data linkage to a specific disease, such as a cancer diagnosis and the related treatments but in addition, to have access to the other non-cancer related conditions and treatments so the effect of co-morbidities can be researched and the overall influence of the treatments determined. This important data linkage can be routinely performed by a biobank with the participant's informed consent whilst still protecting the privacy

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and security of all personal information [2]. Access to the national health department's clinical databases also provides practical and great economies to a biobank whose routine task is to perform clinical follow-up on all recruited participants. The reason being, the national health records database provides the additional clinical history and treatment regimen information that a biobank cannot currently obtain, as it is impractical for the biobank team to know about, or even try to cover, all hospital and/or general practitioner interactions that a biobank participant may have.

Whilst biobanks have been established over many centuries, over the past 15 years as the current facilities have matured, there has been recognition that harmonization and professionalism for all work activities needed to be established globally. This approach has provided benefits and is now allowing researchers and clinicians to advance our knowledge in disease prevention and treatment and translate these research findings to provide better health outcomes for patients. Just as critical when establishing and operating a biobank is an understanding of the public's perception and acceptance of the decision-making process in deciding to be a participant and contribute to a biobank. This requires extra consideration, specifically when it involves a biobank for genomic research [2–4].

One essential activity of a biobank manager is the constant review of the facilities strategic plan to ensure they are always relevant to the market's needs. Incorporated into the strategic planning is the constant engagement and collaboration with academic and commercial researchers and clinicians accessing their resource so that the management team can modify the collection protocol regimes, if indicated. That may include the type of biological sample being collected and the processing, storage conditions of the samples so they are suitable for new technologies being used and the type of linked clinical data. A willingness to frequently review and modify a strategic plan and collection protocols at different time points is essential, as there is no point in spending allocated funds to collect biological samples and data that are never used. In regards to funding, the identification of as many avenues as possible to fund the biobank facility is prudent and this may involve applications and engagement with government agencies, not for profit agencies and philanthropic donations. All forward budgets need to include a plan for sustainability to protect the infrastructure for long term storage, all within the framework of ethics approvals, the legal jurisdictions of where the biobank is located and observance to social acceptance and the research and community needs.

Biobanks have been broadly defined into three major types [5]:

1. Population biobanks where biological samples and data are used to determine markers of susceptibility and population identity, representative of a country or ethnic cohort.
2. Disease focus biobanks (or cohorts) for epidemiology and genomic analysis where the research focus is on exposure and modifier influences using DNA and the large collection of specifically collected baseline and clinical follow-up data. All generated results are frequently compared to a population based healthy control group.

3. Disease focussed general biobanks whose participants provide biological samples and limited clinical data to be used to identify markers for disease. The data in most cases is minimal and baseline and is not collected for a specific research project but is a more speculative collection in nature.

There are many hundreds if not thousands of combinations of the three types of biobanks worldwide and beyond the numerous references in the scientific literature [6–11].

Our understanding of what is required to facilitate translational research and the role a biobank may play for improved patient outcomes is becoming more streamlined and specialist in nature due to experience. In a recent British "gap-analysis" publication of the critical tools needed for translational research to advance the understanding and successful treatment of breast cancer, the authors outlined ten points to be addressed, one of the points being the vital need for the development of collaborative infrastructure (biobanks) that contains clinically annotated and longitudinal biological sampling in patients with this disease, was repeatedly identified [12]. The southern Swedish malignant melanoma research initiatives have also highlighted the gap between the bio-analytical and clinical translation and have developed the required biobank infrastructure with a multi-discipline group membership to provide best practice protocols and procedures for an integrated platform and work flow to advance the understanding and improved diagnosis and treatment in this disease stream [13].

Biobanks can be established as individual entities; however, it is increasingly common for biobanks to contribute their collected resources as part of a national or international network. This enables biospecimens and data to be provided in sufficient numbers for large scale analysis that generates the required power calculations and adequate sample size for biomarker studies, analysis of rare diseases, or small subtypes of common diseases [14–16]. The models available for the establishment of a biobank are also numerous with all models acceptable and best framed around the most suitable conditions related to the geography, social and political landscape. There are two common forms of biobank structures, the first one is a network that is known as a Centralized model where samples and data are collected from staff at potentially multiple sites and transported to a central laboratory and data centre for processing, storage, value adding and distributed to approve research projects. Examples of this are BancoADN, Spain (http://www.bancoadn.org/en/presentacion.htm); kConFab, Australia (http://www.kconfab.org); the Singapore Tissue Network, now the Singapore Biobank (http://www.stn.org.sg); and the UK Biobank (http://www.ukbiobank.ac.uk). The second model is known as the Federated model and is where samples are stored at numerous collection sites and the collections are combined in a virtual sense by transferring sample information to a central database. This allows researchers to identify collections or series of samples of interest and access them from multiple collection sites. Examples include the Australian Prostate Cancer BioResource (http://www.apccbioresource.org.au), the Canadian Tumour Repository Network (https://www.ctrnet.ca), the Wales Cancer Bank (http://www.walescancerbank.com), Tubafrost (http://www.tubafrost.org), as well as the P^3G catalog of large epidemiology based cohorts (http://www.p3g.org). The two models have different

advantages and disadvantages. The Centralized model allows for the storage and processing of samples to be easily controlled and processed and managed in a standardized manner, which is an extremely important benefit. The disadvantage is all health professional contributors need to support having the one site as the overall custodian of the biobank collection. The Federated model is potentially more acceptable to stakeholders at the numerous collection sites because they remain more involved throughout the biobanking and decision-making processes for the samples and data being collected. The disadvantage is the difficulty in processing the biological samples and data in a standardized manner and, delivering the material in a timely, organized, coordinated manner from multiple sites to approved research projects [17]. While a clinical pathology department's primary role is not as a biobank, the clinical diagnostic samples and linked data retained by these facilities are a valuable resource for research. Many of these facilities have been actively involved with biobanking activity and are integral to the operations of the two biobanking models detailed above. This retained resource is an economical use of an established infrastructure that can be made available to researchers for analysis where appropriate approvals are obtained.

Ethical Considerations

A biobank, as the "trusted third party" in any setting involving patients, researchers and clinicians, provides an essential mechanism for separating consent to clinical care from consent to use donated biospecimens and data in research.

In most jurisdictions around the world, oversight of the use of human biospecimens for research is the responsibility of a committee charged with reflecting community norms and ethically defensible opinion on appropriate research conduct. These independent ethics committees, known as Institutional Review Boards (IRBs) or Human Research Ethics Committees (HRECs), commonly have responsibility for monitoring the activity of a biobank at their respective institutions. Very large, national biobanks such as the UK Biobank in the United Kingdom and CaHUB in the USA have established an independent entity to oversee the governance and ethical oversight of their large biobank facilities. In Australia, the National Health and Medical Research Council (NH&MRC) provides guidance to HRECs through the National Statement and has established a registry of committees [18].

Consent

A vital consideration and key to the usefulness of a biobank for future research is the explanation and definition of what the term "consent" means when approaching donors. The goal of informed consent is to ensure that subjects are fully aware of the risks and potential benefits of the research to be performed and make a voluntary decision about

participating in the research. The dilemma facing all biobank facilities is that due to the speed of advances in technology, the future use of the stored biospecimens and data are sometimes unpredictable and not fully articulated at the time of the consenting process. Previously collected biospecimens and data distributed to researchers, sometimes years after the collection, made it difficult, if not impossible, in many cases to describe in detail at the time of the consenting process, what the exact future research of the samples and linked data will entail, or the significance and impact of possible findings. Therefore practically, it is important to recognize that in many cases the legal and ethical requirements of informed consent for all future uses cannot be satisfied at the time the biospecimens and data are collected. Even so, research into the community attitudes about this issue indicate that most participants would agree that stored specimens and data are a valuable resource and should be used to advance research if appropriate protections are in place.

Basically, the type of participant consent gained falls broadly into three categories:

1. Specific consent for use in a defined and finite project;
2. Extended consent for use of biospecimens in research that is related to, or a direct extension of, the original project for which consent was given;
3. Unspecified, broad consent for use in future research. Such consent is usually underpinned by the knowledge that any future research will be conducted under oversight of the relevant ethical oversight committee.

Many ethical oversight committees now consider, in some circumstances, a waiver of donor consent. This option is included on the majority of IRB/HREC application forms in recent times. For a waiver to be granted, in general the following conditions need to be determined:

1. The research involves no more than minimal risk to the subjects;
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. The research could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

In regards to point 1, when a waiver is requested by the researcher, there needs to be consideration by the IRB/HREC about whether research using stored biospecimens and/or data meets the criteria of involving no more than minimal risk. Some have argued that because the risks are primarily informational, as long as adequate privacy protections have been adopted the research should be considered minimal risk. However, research shows that IRB/HREC chairs are not always in agreement of what constitutes minimal risk and tend in the main to be conservative in their judgments. A standardized, global definition of minimal risk in this context would aide researchers and IRB/HRECs in their determinations of whether a particular research project using identifiable specimens or data can go forward with a waiver of informed consent. With point 2 and 3, as long as appropriate security measures are in place and the research does not involve traits or conditions that would be viewed by the subject

or the community to be highly sensitive or stigmatizing, a waiver of consent should not adversely affect the rights and welfare of consented participants. In addition, in many cases granting a waiver to consent is a practical decision as there can be logistical difficulties in re-contacting participants, some might have changed address therefore potentially difficult or impossible to locate or they may be deceased with no next-of-kin details available to obtain a proxy consent. For this reason it is understood that some valid research facilitated by a biobank could not practicably be carried out without a waiver of consent on occasion [19–23].

There has been discussion and some resistance to such a waiver in recent times. The University of California, San Francisco initiated a blog calling for public comment on issues of consent to raise awareness and generate community discussion about research ethics and the use of de-identified biospecimens in genome sequencing activity [24]. Oliver et al. recently conducted a randomized trial of three consent types affording varying levels of control over data release decisions on participants recently recruited into one of six on-going genetic research studies that covered a broad spectrum of diseases and traits. Follow-up interviews were held to assess their attitudes towards genetic research, privacy and data sharing. The results found that participants were more restrictive in their reported data sharing preferences than in their actual data sharing decisions as they saw both benefits and risks associated with sharing their genomic data. Risks were seen as less concrete or happening in the future, and were largely outweighed by asserted benefits [25]. In the discussions around waiver of consent, these studies highlight the ethical conduct considerations when it specifically involves genome research and that proposed policy changes should carefully consider the research participants perspectives, including privacy concerns [26, 27].

Another major consideration for biobank governance and management that has been widely discussed in the literature and tested in law is the question and observance of ownership and secondary use of the biospecimens and data samples [28–30]. In Australia, community and industry views have been important in shaping guidelines for the ethical use of human tissue in research and jurisdictions internationally have also developed positions relevant to local law [31]. Training of biobank management in this area is essential so there is adherence to the legal requirements and statutory guidelines to maintain the public's trust and respect of these facilities. Therefore, when preparing a Participant Information and Consent Form (PICF), a number of broad questions should be considered and addressed:

- Will the biobank collect for future unspecified research?
- Will the biobank supply de-identified, or potentially re-identifiable biospecimens for research?
- Will the biobank return genetic research results of clinical significance to the donor, the donor's nominated family member(s) and treating doctors?
- What is the scope of applications considered by the biobank for access to resources, i.e. would the biobank be open to receive applications from researchers in both the academic and commercial setting?

- What other records or information will be needed. Does the biobank plan to acquire clinical or other data to annotate specimens through linkage with other, external national or international databases?
- Will the collected de-identified data potentially be downloaded and pooled with other similar external research groups?

Including the relevant clauses in the PICF at the establishment phase of the biobank operations will deliver the most efficient and cost effective ethical framework under which to operate the biobank and be ethically compliant.

Consideration must also be given to the legal and ethical framework of the jurisdiction in which the biobank operates as we are increasingly moving towards international collaborations so it is essential that the elements of consent under which biospecimens and data are collected are robust to allow sharing of this material across international borders. The guidelines and policies established by The International Cancer Genome Consortium (ICGC) on informed consent and access policies were specifically drafted to address the requirements of an international genome wide sequencing project. The elements of informed consent described in this document are an excellent guide to produce a robust and enduring consent document for biobanks in the genomic age [32].

Translational work is being performed by cancer genetic cohort research studies that collect blood for germ-line mutation identification. When personally relevant genetic information is discovered, established protocols are in place to notify participants of these clinically significant, research generated mutation test results. With the best intent by the researchers and clinicians involved in these cohorts, and a confirmed indication from the participants when they were recruited into the genetic research study that they wanted to be notified of clinically significant mutation test results, it remains to be a challenge to effectively notify participants from high risk cancer families, and increase the proportion whose risk is managed clinically, particularly for males and individuals unaffected by cancer. Improving notification of at-risk cancer individuals is an important goal in both the research and clinical environment. Further investigation of the potential barriers to communication between genetics research groups, family cancer clinicians, at-risk individuals and their family members is urgently needed. The ethical implications of these types of studies are also important, and highlight issues for further discussion in the genetics community. A key ethical question does remain unanswered: “If research studies are obliged to notify participants when new genetic information becomes available, to what lengths should they go to meet these obligations?” This question also raises important financial and logistical considerations regarding how many resources research studies should (and can) use to notify their at-risk research participants involved with a biobank or cohort study [33].

The other important issue to be considered and addressed when developing the PICF is when researchers accessing the resource are conducting genetic research that has the potential for finding a heritable genetic alteration that is incidental to the purpose of the analysis or research, and may be considered by a research participant, a clinician or the researcher to be of significance to the health or reproductive

decision making of the research participant or their family. This is particularly true of research involving whole genome sequencing (WGS) or any high throughput research techniques that have the potential to generate incidental findings of heritable genetic alterations. Incidental findings (IFs) are made in the course of conducting research, but are, by definition, beyond the aims of the research project. IFs may or may not be anticipated and researchers and others may disagree about their validity, reliability, significance and need for reporting back to the participant.

Whether researchers have a moral obligation to provide findings of this nature back to research participants is a vexed issue with an international consensus just starting to be defined [34, 35]. The matter is complicated by the fact that, unlike clinically validated genetic tests, WGS and other high throughput research techniques are research tools, that is they are not designed for clinical diagnosis and they produce results that are of questionable clinical utility and difficult to validate. Results from these analyses may identify genetic variants that are related to increases in disease risk, but the increased risk may be particularly small. Further, genetic associations that are found may well be non-replicable or difficult to interpret. Nevertheless, findings that are currently uncertain may in future become clinically relevant. Accordingly, the identification of an IF raises questions regarding the potential need for evaluation of the finding and for communication to the participant's clinician or to the participant. One recent study examined the attitudes of individuals diagnosed with sarcoma and their family members towards genetics, genomic research and incidental information arising as a result of participating in genetic research. The results demonstrated that no matter whether they were individuals affected with cancer or their family members, they were generally positive about new genetic discoveries and genetic testing. Possibly not surprisingly, age and gender were factors that influenced how people thought about genetic discoveries and genetic testing. Although intention to receive results did not necessarily translate into action by attending a clinic to obtain their personal genetic test results, the research team believe that if genetic testing for sarcoma becomes available in the foreseeable future, it is likely that family members may demonstrate more reservation towards such testing than the cancer affected and their spouses and this should be taken into consideration. Finally, the majority of sarcoma participants believe people would like to be informed about incidental information arising as a result of research [36].

For these reasons, developing management pathways between the researchers, biobank management and the local IRB/RHEC to determine whether or what information should be feedback to research participants, their families, or clinicians involved in their care and who should be responsible for feeding back these results is necessary. More research in this area about decision-aids to notify participants and evidence based research on attitudes and what is understood by the participants who are signing consent forms to be engaged in this area of researcher is essential. The PICF or other information designed for presentation to research participants should be designed, as a minimum, to clarify that, in the course of the research, information may arise suggesting the presence of mutations that are unrelated to the specific disease or trait being investigated [37].

Sustainability

Whether a biobank, cohort or registry is established with a defined participant recruitment criteria to address a specific research question, or is a speculative collection with the view for future use, the issue of sustainability for the estimated life of the resource that includes procurement, sample processing, data linkage, value adding, clinical follow-up, maintenance, infrastructure and the supply chain for distribution needs to be addressed with all management and operations scoped before a facility is started. Establishing such facilities, even small ones, is a very expensive operation [6, 10, 38–40] (Table 1). Funding for such facilities can be sourced from one or a combination of organizations: not-for profit granting agencies, universities and research facilities, government, private foundations, commercial biotechnology and pharmaceutical companies. In addition to the financial commitment, sustainability may also require long term support and commitment from the donor participants to provide updates about clinical information and biological samples as new diagnosis and treatments are made. The on-going interaction and communication strategies between the biobank management and donors are an important demonstration that the facility is adding to our knowledge base about the population that has been recruited and is beneficial and rewarding to all parties. Such interaction

Table 1 Costs in establishing a bio-bank facility

Facility name	Funding source	Funding received	Years funds awarded	Facility size
Australian (Oncology only) enabling grants	Federal Government (NH&MRC)	Aus$ 22 million	2004–2014	Medium, 12 independent networks
The pan-European Biobanking and Biomolecular Resources Research Infrastructure—European Research Infrastructure Consortium (BBMRI-ERIC)	National governments	€135 million	2013	Large, 10 networked counties
caHUB, NCI, USA	NCI	USA $23 million	2009	Large, numerous networks
Israel National Biorepository	National government and philanthropy	$10 million	2008–2013	Small, numerous networks
Stellenbosch Biobank H3Africa—H3Africa Consortium	National and International government	$74 million	2012–2018	Large, numerous networks
UK Biobank	Numerous national and regional government and not for profit organizations	£87 million	2006–2016	Large, numerous networks

can be invaluable in highlighting a biobanks aim and purpose to funding agencies. When establishing a facility it is important to recognize in the budget projections that most biological samples linked to data become more valuable for research purposes after 5–10 years of clinical follow-up, often with repeat sampling of biological material and data. Exploring all options to ensure that the collected material is used to facilitate research is essential, for example, biological samples and data may have been collected originally for a specific project with the samples embargoed until that research project is completed. At the completion of that project the remaining samples, excess to the original project's needs, will be free to be used by other groups, potentially with the value added data generated from the original projects findings. Therefore, when determining the overall costs for sustainability it is important to capture all expenses that include the costs for the initial set up and the on-going operational costs, on average 15–20 years, for management and laboratory staff, laboratory facilities, equipment and maintenance, databases, supply of material to researchers and data linkage to external agencies such as cancer agencies, medical records and health departments, as the facility matures.

Government and not for profit granting agencies will frequently provide funds for the establishment of a biobank, cohort or registry but unfortunately, it is frequently the case that the agencies then fail to recognize that on-going funding, even at a small percentage of the original grant total, is still required to fund the existing infrastructure to maintain the facilities operations, even when co-funding from other organizations and cost recovery schemes are in place. A common occurrence appears to be that at best, biobank facilities can obtain 5–10 years of funding before being informed that they need to be 100 % self-sufficient by their funding agencies. For biobank facilities who are relying on predominately academic researchers funded through peer review government awarded grants, being 100 % self-sufficient by the implementation of a cost recovery scheme isn't an achievable goal as the researchers grants are usually lean in value and committed to other aspects of their research project. Academic based researchers do not have grant funding anywhere near the levels required for a reasonable cost recovery linked to the true collection and supply cost. In addition, the demand to supply biological samples and data held by a biobank and linked to a cost recovery fee can vary year to year, sometimes dramatically. This makes budget predictions based on a cost recovery scheme alone very difficult and not sustainable.

Linked to the issue of biospecimen and data usage and sustainability, it is important at the facilities establishment stage to understand what the market requirements are and the potential demand so to optimize the use of the collected resource. The strategy of collecting all surgical material in a speculative manner in the hope that it might be used at some stage has led, in the majority of cases, to a very small percentage of usage of the collected material. A more strategic plan can be seen where the biobank is embedded within the clinical pathology department as the biological samples and associated pathology and treatment data have already been collected for clinical diagnostic purposes and eventually will be available for research purposes when deemed to be in excess to diagnostic purposes [40, 41]. The other productive model is associated with the cohort biorepositories and registries where

there is often a rich collection of biological samples such as multiple sampling of tissue, primary and metastatic, and blood from the recruited participants. The biological samples and data in a cohort facility have usually been collected to support a series of specific research questions. The associated data may have been collected for 10 years or more linked to comprehensive epidemiological and clinical follow-up data. The cohorts traditionally demonstrate flexibility in its expansion of sample and data collection as the specific clinical and scientific aims of the cohort study evolve [42–44] with a large percentage of the biological samples and associated data used by research approved groups multiple times.

A recent review of 636 biobanks in the USA characterized their origins, specimens collected, market context and the issue of sustainability. Importantly, linked to the issue of sustainability, the researchers found that having a biobank embedded in a larger organization, such as a hospital or research institution, was essential to the biobanks financial structure and survival. The majority were associated with an academic institution 78 %, hospitals or research institutions 27 % and 15 %, respectively.

When the biobanks were asked about how competitive they were in the market place, only 14 % answered in the affirmative. Significantly, only 4/57 (7 %) of the biobanks stated that there was a "great deal" of competition for their resource, 51 % stated a modest amount and 42 % indicated that they had very little competition. They found that *for profit* biobanks were significantly more likely to be competitive (61 % vs. 12 %) and it appeared that most of the biobanks surveyed filled a specific niche within their organization and were not concerned about holding the share of their "market". In response to a question about the demand for their collected facility products, 51 % reported that demand for their biobanks products had increased over the past 2 years, 6 % found demand for material had decreased and 45 % answered that it had remained about the same. In the current period of financial restraint, it was a surprise that only 13 % of biobanks had a major concern about the under-utilization of their resource, 28 %, respectively, had moderate or minor concerns while for 31 % of biobank facilities it was not a concern at all [7].

As on-going funding for such facilities is a recognized challenge internationally, options for sustainability have led to many funding avenues being explored and adopted, depending on the local funding landscape. By far the best and potentially easiest option is to have the host institute fund the facility 100 %, and for the facility to become part of the health care structure of the institute. From a practical sense this model is best suited to a smaller, single site type of facility as the political logistics of funding sourced from a single site to support a multi-site network where numerous sites collect and pool their samples and data is problematic. In the expanded, multi-site collection model, ultimately one site from the group will have the responsibility for specimen and data collation and responsibility for the facilities management. The challenge for the management of a multi-site networked group is to convince a local hospital or research institutions management where the centralized facility is based that funds should not just support the local sites collection but that part of the funds are needed to support the broader networks activities to collate, value add and distribution the biobanks material.

Whilst there are many valid arguments about the merits for the consolidation of biobank activity across networks with standardization being the essential aim for best practice and efficiency, unfortunately, the funding required to support this type of centralized, broader network is rarely taken up by one sole institute due to that organizations own budget restraints, legal nuances and other competing interests within that groups health structure. In the current financial climate, largess is becoming harder to find in publically funded organizations. Fortunately there are a few good examples of regional and inter- and intra-country networks that have managed to resolves many of these problems and established medium to large scale facilities receiving a combination of government, not for profit and foundation funding [6, 10, 14, 38, 44, 45] to support their combined networks.

As previously mentioned, another popular model for sustainability is the leverage of a cost recovery or administration fee. Many facility managers strongly argue that even if a facility has 100 % funding coverage for all aspects associated with the operational, logistics and supply costs, a small fee labelled as an administration or cost recovery fee that is associated with the managers time and for a small portion of the costs associated with the collection and value added component of the biological material or data being supplied can be a useful tool as it makes researcher accessing the resource think responsibly about what material they are requesting. This fee also assists in avoiding inappropriate or over ordering, therefore, wastage of the valuable biological samples. In addition to an administration fee, the dilemma for all biobank facility managers is how to structure a cost recovery fee that takes into account the original cost to recruit and consent a participant, collect the relevant biological material and data, value add and supply to an approved research project, hopefully multiple times. Against this value, and already mentioned in this article, is the realistic cost that a researcher wishing to access the resource can afford to pay, especially if they are an academic researcher on a modest government awarded research grant that needs to cover multiple laboratory wages and consumables and where there has not been an allocated budget to access a biobanks resource due to a research project evolving. In addition, most biobanks in the not for profit arena need permission from the relevant government authority to charge a cost recovery fee and certainly are not allowed to make a profit from the supply of material to an approved research project [46]. When dealing with a private or industry partner, the regulations in some countries are even stricter in regards to the implementation of a cost recovery fee [6]. Cost recovery charges are usually reviewed annually and adjusted, if need be, to reflect the level of grant funding from other sources. At best, internationally most biobanks would only be recouping 10 % of their total budget costs related to recruitment and on-going overheads.

Though small in number, economic models have recently been developed around using centralized consolidated biobank resources to produce budget savings and efficiencies to aid the long term sustainability of these facilities. The prepared economic model provides a more accurate estimation of direct vs. indirect biobank costs and establishes the cost effectiveness and cost benefit evidence that is required to justify, usually to government, spending in this area. Variable and fixed costs, cost recovery schedules that incorporate internal and or external funding sources, access fees,

administration infrastructure costs and potentially intellectual property considerations have all been built into these models. The authors hypothesize that these models will lead to analysis efficiencies, improved data accuracy and infrastructure costs, therefore, improvements in patient welfare and a higher professionalism within the work place and sustainability [47]. The authors also highlight the practical aspect of an efficient biobank, that is, it isn't the number of samples that are collected and stored but rather how many samples are out going to support research projects, making sure that you do have a "product" that the market wants, and ensuring that the biological material and data is of the highest quality possible. Linked to this is the aspect of a cost recovery fee that can be modified at any stage, that is, "stepped" or "graduated" as the collection matures, or funding streams become available or cease, hence a developing business model over time to ensure the sustainability and protection of a vital resource [48]. Another funding revenue source that has also been increasingly adapted by biobank facilities in recent times is a contracted service fee offered by research groups and pharmaceutical companies who want a patient group recruited with specific biological samples and data collected under strict collection protocols. There are economies for all involved by *piggy-backing* onto this type of customized service as a business model. The down side is that the biobanks main collection and recruitment may be reduced as the contracted service takes up the biobanks routine scheduled work time, but at least it secures another streaming of funding to keep the facility operational. Whilst the majority of biobanks are supporting academic research groups, facility managers should be aware of the demand for well-annotated biological samples linked to clinical, genomic data and treatments that can be used by pharmaceutical companies for drug discovery and validation analysis. In determining a cost recovery fee to be charged to academic researchers vs. commercial research groups, academic researchers may argue that a public biobank that has been funded in the main from a government grant whose revenue has been obtained from public taxes should not be charged all, whereas private commercial entities who have the ability to pay for access to the resource, due to the potential profit generated, should be required to pay a higher cost recovery user fee. This is not an easy issue to manage, especially against the background of lower government grants to fund biobank facilities in recent time. Overall, there does appear to be consensus that it is reasonable and fair that the cost recovery schedule for the supply of biological samples and data to an academic researcher is less in value than to a commercial company and charging all of the groups that access the resources, thereby, the established infrastructure in the public domain to advance their own interests promotes an equitable approach for the financing of public funded programs [44, 48].

Best Practice and Access Protocols

The protocols around sample collection are driven by a number of factors as not all biobanks have the same brief. A biobank may focus on specimens collected during routine clinical care for therapeutic or diagnostic purposes that are then in excess to

clinical purposes, specimens collected for clinical trials, specimens collected as part of specific research projects or specimens collected as part of population based or cohort biobanks.

Collections for a specific research question will be built around the methodology developed by the researchers although whatever the biobanks design and function is, harmonization of biobank operational procedures and a recognition of international best practices is an essential requirement for the management and all staff. As the diverse types of biobanks in existence have different roles in their operations and translation of the generated research results, there is also a recognition that it impossible and potentially undesirable to harmonize completely all practices, policies and operations [49]. It is essential though that the biobank manager and staff recognize when complete adherence is or isn't required, for example, in the era of large scale global collaboration that requires the exchange and pooling of data and samples, exacting standardization of SOPs and harmonization ensures the effective interchange of valid information and samples from numerous groups to be pooled for analysis [50]. There are many excellent papers and documents listing extensive descriptions of appropriate collection protocols and SOPs developed by peak biobank groups over many years [8, 51–53]. As well as their documents being a practical resource for day to day use, these protocols also provide confidence to funders, participants and researchers accessing the resource. One dilemma that is currently being discussed and urgently needs to be addressed by all biobank facilities is the fact that researchers are highlighting that they are having trouble accessing sufficient numbers of samples from a biobank and that the available samples are not always suitable for their research purpose. From the biobank operational and usage milestones, they have 1000s upon 1000s of biospecimens and data stored that no one is using. This is one of the issues that the ESBB working party (http://www.esbb.org) is currently addressing (personal communication with Drs Dominic Allen and Christina Schröder) with the development of a register of all biobanks that list their specific features. This is to be followed by a greater dialogue between the biobanks, academic and commercial researchers to help identify and solve collection and supply issues between all parties. Linked to the problem of previously collected biological samples not being fit for purpose, or having an under developed matched data set, in recent times it has become common for the research departments of pharmaceutical companies to contract a biobank to collect the samples required for a defined research protocol. There is still a problem with this strategy as the challenge then lies in recruiting enough participants and collecting enough biospecimens linked to clinical follow-up data in a prompt and reasonable time frame, i.e. what was the response to a first line treatment regime that may be administered over a 6–8 month period.

The final governance issue for the biobank management to address is the development of a policy and procedures document that clearly outlines how to access the biobank resource to facilitate research in a transparent, effective and equitable manner. It is also important that these documents are visible and easily located so external researchers can see what biospecimens and data are available and what the formal application process is to access the material. Establishing such policies and procedures can be a challenge as obviously some of the stakeholders involved in

establishing the biobank will have a legitimate and positive vested interest in establishing the infrastructure as it will bring a productive flow of material and data to their personal research work. The handling of potential conflict of interest (COI) does need to be addressed and worked through. Many groups have resolved the COI issue by establishing a working committee that includes multi-discipline professionals with a wide range of relevant specialties and that includes community representation. There also needs to be a recognition and a willingness by everyone in the organization and stated in the groups Terms of Reference (ToR) that members will be excused from discussions and decision making if a COI is evident or perceived. The primary aim for the whole organization is to provide access to the biobank resource to everyone, internal and external investigators, who apply and who has an IRB/HREC approved project linked to a peer reviewed research study that is funded. Operationally, it is important that all applications are reviewed formally and all decisions documented. This can be achieved by researchers submitting a research proposal to the biobank management that outlines the research aims, hypothesis, plan and conclusion, the overall number of participant numbers required and the specific amounts of biospecimens and data points and suggested timelines for the supply of material. Proposals can be reviewed and commented on by a sub-committee with expertise in the field of interest. Once all questions and concerns about the project application are addressed, the project can be approved. It is essential at this stage that the researcher accessing the resource is aware of the terms and conditions required to access the biobank resource. Practically this can occur in a formal project acceptance letter that may include requirements such as the submission of annual progress report, the length of the project approval period, depending on the circumstance the signing of either a Material Transfer Agreement (MTA), Memorandum of Understanding (MOU) and Data Transfer Agreement (DTA), acknowledging the biobank in all publications and the return of all generated research results back to the biobank after publication. This last step is an invaluable data adding contribution from the researcher to the overall data held by the biobank facility and has the added benefit of avoiding duplication of research efforts on the precious biological samples. The same requirements have been applied when a biobank or researcher accessing a biobank resource then contributes to another consortia with a new set of MOU, MTA and DTA agreements being signed to protect all stakeholder's interest. Whilst non-compliance to the ToRs by researchers accessing a biobank resource is thankfully uncommon, it is important for the biobanks policy and procedures document to state what penalties will be enforced should any access policy and procedure requirements be broken.

Quality Assurance and Quality Control

It is essential that a biobank incorporate a quality assurance (QA) and quality control (QC) programme into their routine work so the facility managers are observing the international best practice guidelines and the programme requirements are meet to

achieve the highest standard possible for the supplied biological samples and data for research projects [54–58]. Robust QA and QC protocols will ensure that the biobanks management group is aware of what specimens and associated data has been received, the relevant transport conditions, the multiple samples that have been processed and stored and what has then been supplied to approved research projects. Researchers receiving the biological samples and data need to be confident that the materials they have received are of high quality and able to support their planned research projects. The process through which the product is obtained is referred to QA, whereas the product generated is part of the QC. For example, quality assurance is defined as "that part of quality management that focuses on providing confidence that quality requirements will be fulfilled" [59]. QA requires the systematic monitoring and evaluation of all aspects of the biobank processes; it covers the way in which the biobank is operated as well as the quality of the samples and data held. QC consists of specific tests defined by the QA programme to be performed to monitor procurement, processing, preservation and storage, specimen quality and test accuracy. These tests may include but are not limited to: performance evaluations, testing and controls used to determine the accuracy and reliability of the biobank equipment and operational procedures as well as monitoring of the supplies, reagents, equipment and facilities. Standard operating procedures (SOPs) are an essential part of quality assurance; a biobank will determine and document its ways of working to ensure that samples and data are collected and handled consistently. As the global biobank community matures, most of the different facilities have shared and published their SOPs to further standardize what is being done in QA and QC. This has been a benefit for researchers receiving samples from different biobanks as there is a degree of confidence that all of the samples will be of a similar quality and for facility managers who are starting to establish a biobank facility [8, 52, 60, 61].

As published by the NCI Best practices in 2007 and revised in 2011, and adopted by many biobank facilities internationally, QA and QC should address the following:

Facility Infrastructure

Equipment validation and change control, calibration, maintenance, repair procedures and environmental monitoring; e.g., temperature monitoring of freezers.

Supplier management programmes, including inspection and validation of reagents and other supplies.

Biospecimen Control and Documentation

Control of biospecimen collection, processing and tracking.

Documentation of biospecimen collection, processing and tracking, with detailed annotation of pre-analytical parameters.

Measurement and analysis of key process indicators to drive quality improvement.

System Security

Recordkeeping and document control.

Employment of a data quality management, assessment and reporting system.

Clinical Data Records

Accessibility of policies and procedures.

Documentation records, including audit reports, deviation reports and corrective action and preventive action reports.

External document monitoring to ensure that the facility remains up to date with relevant laws, standards and best practice publications.

Staff training records, including record of staff adherence to training schedules.

Data quality management (source documentation and electronic records), assessment of reporting system.

Supply Records

Internal audit of program and its policies, scheduled and unscheduled.

Audit for accuracy of all annotation data; e.g., the biospecimen and where it is purported to be, in the purported volume, with the appropriate labels and unique identifiers.

Audit for accuracy of patient data associated with biospecimens; e.g., age, gender, date of diagnosis and processing, etc.

Audit of the compliance of the biospecimen resource with institution policies; e.g., human subjects and privacy and confidentiality protections, prioritization of biospecimen use.

Audit of SOPs for all activities, processes and supply.

Each biospecimen resource ensures that SOPs are written, reviewed and are an appropriately approved process that exists for review and updating at designated time intervals.

In addition to the best practice guidelines published by the NCI in recent times, as many biobanks have matured they have been innovative in the era of molecular pathology and genomics to also include a rich collection of phenotypic data and comprehensive clinical follow-up data linked to each biological samples. This extra data value adding via these new technologies has led to the biobank facility sharing new genomic platforms either within or external to their work site for high throughput technology to derive data for bio-informatics analysis. A key requirement for data to be analysed when samples and data have been pooled from multiple sites depends on harmonization and standardization of SOPs have been developed and used by all of the contributing biobanks so uniform, combined data analysis can

occur. In recent times there are good international examples where cancer consortia have agreed on harmonized SOPs so large scale analysis can occur to gain the required statistical power for analysis [62, 63]. In these multi-site global consortia, biological samples being supplied such as DNA or RNA undergo rigorous QA and QC using concentration determination methods best suited to the platform technology being used, i.e. picogreen or qubit readings for DNA concentration are often used in preference to nanodrop for Next Gen Sequencing or whole genome Copy Number Analysis. For the supply of fresh or archival tumour tissue, researchers will often request to know the % tumour, stroma, ducts and necrotic tumour in every specimen before deciding on the optimal case with the best cellular component for their analysis [64]. Using a scanning microscope to capture and catalogue the tissue image also aids external researchers in deciding the tissue they wish to access by having log in rights to view the scanned tissue. This process has provided a speedier supply of tissue for review, and eliminated the hazards and delays associated with the shipment of glass slides to external sites [65].

Whilst it is a challenge to implement flexibility and adaption for biospecimen SOPs to address the needs of emerging technologies, a lack of attention to SOPs and adjusting the SOPs for a project requirements in molecular pathology research can lead to misconception of molecular findings and discrepant results if the sample being tested isn't of a high quality, contains contaminants or has not been prepared under the appropriate protocol. Having the correct specimen characteristics, prepared under standardized SOPs that includes stringent QA and QC, is the recognized way to advance translational research.

Databases

In addition to the acquisition of biospecimens and data, the other important item in the SOPs is the purchase or development of a database so that the entry of all of the items associated with the biological samples linked to a data dictionary are entered for every participant recruited. With the evolving technology and laboratory findings translated into clinical practice, it is also important to consider when purchasing or developing a database that upgrades and modifications may need to be made within a few years of purchase due to the extension of the data dictionary to record additional data parameters or potential linkage with other groups due to data sharing. Awareness of the international standardization and published protocols for specimen and data collection is required so compatible data fields are implemented. Analysing data generated from biological samples and clinical data is becoming more complex as combined datasets become larger due to the new technologies and data sharing of multiple groups to gain statistical power. Therefore, databases are integral to performing the required large scale analysis to understand a complex disease such as cancer. Depending on the nature of the biobank, databases can be purchased off the shelf or purpose built. A database provides not just management, operations, governance and details of the researcher access approval, but they also enable the results that have been generated on the supplied samples to be

downloaded back into the database as a value adding exercise for further analysis. Tracking of this information manually is not practical and in fact impossible to do, especially with the larger networked consortia, without a database. It also ensures that specific data searches can be performed to avoid duplication of work and locate a required sub-set of biological samples. There are many international examples of where supplied biological samples and/or data to a researcher are returned back to the facility after publication by the researcher [44, 66]. A good practical example of this activity is when a researcher might perform immunohistochemistry (IHC) using a panel of antibodies on supplied tissue. These IHC results can be returned to the biobank and entered into the facilities database and then made available to other researchers with the same research question.

All countries have laws and guidelines for the security of information entered into a database to protect privacy and confidentiality of the participants to protect and minimize accidental or intentional abuse. In most cases participant's identifiable information can't be entered into a biobank database without a participant's acknowledgement and approval although these requirements can vary between regions and countries [67–70]. A database containing information should have the information held on servers at a secure site and be password protected. This security aspect has become even more important now that many databases are web based and accessed via multiple sites. SOPs should include specific guidelines for frequent staff training about all aspects of best practice in regards to the information entered into the database with adherence to the privacy and confidentiality laws and guidelines for their location or country whilst facilitating the researchers' needs for appropriate biospecimens and data [71, 72].

Recently developed databases can generate a de-identified number that can be used when supplying material to researchers but that can be decoded, if required, by the biobank staff. Many cohort studies also have the ability to generate via their databases a unique family specific number when multiple family members are recruited into familial cancer research studies. The decoding of the de-identified number by the biobank staff is a practical function as it means in addition to the baseline data collected at the recruitment phase, clinical data from external facilities, such as the death and cancer registry, hospital discharge diagnosis data, general practitioner data; medication prescriptions, pathology reports, imaging reports, screening practices and health-related data can be linked at any stage which greatly adds to the depth of the data available for research purposes. The external number of all clinical procedures should also have been entered into the database, if possible, so contact with the clinical service can be made if extra treatment details are required.

Equipment and General Requirements

It is difficult to be to prescriptive about what equipment is required for a biobank as variation will occur depending on the scope of the facility. SOPs have been published by all of the major groups such as ABNA oncology, BBMRI, ISBER and the

NCI on general requirements. In brief, all groups agree that thorough planning and resource design is required so suitable space is available for equipment such as freezers that includes −20, −80 and liquid nitrogen banks, bio hazard hoods and centrifuges all with automated alarm systems in place to alert the staff of equipment failures. Linked to this is the need for maintenance, delivery, warranty, service contracts, lifespan, performance and efficiency cost savings, along with current and future service provision options. The depreciation for all capital equipment and replacement costs need to be factored into on-going budgets.

As part of the QA/QC protocols and to ensure the best conditions possible for the biological resource, all maintenance visits and routine staff checks for equipment should be scheduled for and be logged into the dedicated files and cover validation and change control, calibration, maintenance, repair procedures and environmental monitoring; e.g., temperature monitoring of freezers. Contingencies plan also needs to be in place and part of the SOPs for back up equipment should there be equipment failure, especially for freezers and liquid nitrogen vats.

Conclusion

After 15 years of a professional approach to the operations associated with biobanking, it has been demonstrated that these facilities have more than just the potential to be a major infrastructure to facilitate a range of benefits for improved health benefits for our community. Global efforts are already utilizing biobanks that are leading to translation of new research findings. Harmonization by biobanks is recognized as being crucial in order to make facilities more robust, targeted and economical that is associated with the important issue of sustainability. The efforts made by the various professional biobank groups have led to a high observance in the development of policies and procedures in the design and management of biobanks, the SOPs for sample handling linked to QA and QC, database entry and data cleaning, all within the national and international ethico-legal frameworks. As research funding for all activity becomes more difficult to secure, one of the biggest challenges for biobanks is to keep networking and forming strategic alliances between governmental bodies, funding agencies, public and private science enterprises and other stakeholders to keep the importance of our work on the agenda.

References

1. Parks A (2009) Biobanks. 10 Ideas changing the world right now. Time Magazine, March
2. Australian Government (2011) D.o.H. Factsheet Medicare Australia pdf
3. Etchegary H et al (2013) Community engagement with genetics: public perceptions and expectations about genetics research. Health Expect
4. Ahram M et al (2014) Factors influencing public participation in biobanking. Eur J Hum Genet 22:445–451

5. Riegman PH et al (2008) Biobanking for better healthcare. Mol Oncol 2(3):213–222
6. BBMRI (2013) Biobanking and Biomolecular Resources Research Infrastructure. November. www.bbmri.eu
7. Henderson GE et al (2013) Characterizing biobank organizations in the U.S.: results from a national survey. Genome Med 5(1):3
8. Network ABNA. http://www.abna.org.au
9. Network CTRnet. https://www.ctrnet.ca
10. UK BioBank http://www.ukbiobank.ac.uk
11. The Cancer Human Biobank – NCI. https://biospecimens.cancer.gov/programs/cahub
12. Eccles SA et al (2013) Critical research gaps and translational priorities for the successful prevention and treatment of breast cancer. Breast Cancer Res 15(5):R92
13. Welinder C et al (2013) Establishing a Southern Swedish Malignant Melanoma OMICS and biobank clinical capability. Clin Transl Med 2(1):7
14. Watson RW, Kay EW, Smith D (2010) Integrating biobanks: addressing the practical and ethical issues to deliver a valuable tool for cancer research. Nat Rev Cancer 10(9):646–651
15. Michailidou K et al (2013) Large-scale genotyping identifies 41 new loci associated with breast cancer risk. Nat Genet 45(4):353–361, 361e1-2
16. Curtis C et al (2012) The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups. Nature 486(7403):346–352
17. Hewitt R, Hainaut P (2011) Biobanking in a fast moving world: an international perspective. J Natl Cancer Inst Monogr 2011(42):50–51
18. https://www.nhmrc.gov.au/health-ethics/
19. McGuire AL, Beskow LM (2010) Informed consent in genomics and genetic research. Annu Rev Genomics Hum Genet 11:361–381
20. Bathe OF, McGuire AL (2009) The ethical use of existing samples for genome research. Genet Med 11(10):712–715
21. White MT, Gamm J (2002) Informed consent for research on stored blood and tissue samples: a survey of institutional review board practices. Account Res 9(1):1–16
22. Wendler D et al (2005) Quantifying the federal minimal risk standard: implications for pediatric research without a prospect of direct benefit. JAMA 294(7):826–832
23. Shah S et al (2004) How do institutional review boards apply the federal risk and benefit standards for pediatric research? JAMA 291(4):476–482
24. Bernard Lo M. The Research Ethics Blog. http://accelerate.ucsf.edu/blogs/ethics/biobank-genomics-research-do-we-need-patient-consent
25. Oliver JM et al (2012) Balancing the risks and benefits of genomic data sharing: genome research participants' perspectives. Public Health Genomics 15(2):106–114
26. Hudson KL (2011) Genomics, health care, and society. N Engl J Med 365(11):1033–1041
27. Pullman D et al (2012) Personal privacy, public benefits, and biobanks: a conjoint analysis of policy priorities and public perceptions. Genet Med 14(2):229–235
28. Gaffney EF, Madden D, Thomas GA (2012) The human side of cancer biobanking. Methods Mol Biol 823:59–77
29. Allen MJ et al (2010) Human tissue ownership and use in research: what laboratorians and researchers should know. Clin Chem 56(11):1675–1682
30. Hakimian R, Korn D (2004) Ownership and use of tissue specimens for research. JAMA 292(20):2500–2505
31. Commission ALR (1996) Essentially yours: protection of human genetic information in Australia. http://www.alrc.gov.au/publications/essentially-yours-protection-human-genetic-information-australia-alrc-report-96
32. ICGC. Goals, structure, policies and guidelines. http://icgc.org/icgc/goals-structure-policies-guidelines
33. Wakefield CE et al (2013) Improving mutation notification when new genetic information is identified in research: a trial of two strategies in familial breast cancer. Genet Med 15(3):187–194

34. Appelbaum PS et al (2014) Informed consent for return of incidental findings in genomic research. Genet Med 16:367–373
35. Viberg J et al (2014) Incidental findings: the time is not yet ripe for a policy for biobanks. Eur J Hum Genet 22:437–441
36. Young MA et al (2013) The attitudes of people with sarcoma and their family towards genomics and incidental information arising from genetic research. Clin Sarcoma Res 3(1):11
37. Issues (2013) Anticipate and communicate. Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts. December. http://www.bioethics.gov
38. National Health and Medical Research Council A (2009) Outcomes enabling grant funding rounds. https://www.nhmrc.gov.au/grants-funding/outcomes
39. Vaught J, Rogers J, Myers K, Compton CC (2011) An NCI perspective on creating sustainable biospecimen resources. JNCI Monogr (42):1–7
40. Watson PH, Wilson-McManus JE, Barnes RO, Giesz SC, Png A, Hegele RG, Brinkman JN, Mackenzie IR, Huntsman DG, Junker A, Gilks B, Skarsgard E, Burgess M, Aparicio S, McManus BM (2009) Evolutionary concepts in biobanking – the BC BioLibrary. J Transl Med 7:95
41. Kaye J (2012) Embedding biobanks as tools for personalised medicine. Norsk Epidemiologi, pp 169–175
42. Henderson GE, Cadigan RJ, Edwards TP, Conlon I, Nelson AG, Evans JP, Davis AM, Zimmer C, Weiner BJ (2013) Characterizing biobank organizations in the U.S.: results from a national survey. Genome Med 5:3
43. NCI (2013) Epidemiology and Genomics Research – cohort consortium. http://epi.grants.cancer.gov/Consortia/cohort.html
44. consortium k (1997–2013) kConFab: A national consortium for research into families at high risk of breast cancer. www.kconfab.org
45. ACC (2012) T.F.H.C.R.C.-T.A.C.C. http://www.fhcrc.org/en/labs/phs/projects/asia-cohort-consortium.html
46. Australia TVG (1982) Human Tissue Act, D.f. Health, Editor
47. Rogers J, Carolin T, Vaught J, Compton C (2011) Biobankonomics: a taxonomy for evaluating the economic benefits of standardized centralized human biobanking for translational research. J Natl Cancer Inst Monogr 2011(42):32–38
48. Vaught J, Rogers J, Carolin T, Compton C (2011) Biobankonomics: developing a sustainable business model approach for the formation of a human tissue biobank. J Natl Cancer Inst Monogr 2011(42):24–31
49. The Wellcome Trust (2011) Sharing research data to improve public health: full joint statement by funders of health research. The Wellcome Trust, UK, 10 January 2011
50. Fortier I, Doiron D, Burton P, Raina P (2011) Invited commentary: consolidating data harmonization—how to obtain quality and applicability? Am J Epidemiol 174:261–264
51. OECD Organization for Economic Cooperation and Development (2010) OECD guidelines on human biobanks and genetic research databases. Eur J Health Law 17:191–204
52. ISBER (2012) Best practices for repositories. Collection, storage, retrieval, and distribution of biological materials for research. Biopreserv Biobank 10:79–161
53. NCI (2011) Best practices for biospecimen resources. http://biospecimens.cancer.gov/bestpractices/2011
54. Betsou F, Gunter E, Clements J, DeSouza Y, Goddard KA, Guadagni F, Yan W, Skubitz A, Somiari S, Yeadon T, Chuaqui R (2013) Identification of evidence-based biospecimen quality-control tools: a report of the International Society for Biological and Environmental Repositories (ISBER) Biospecimen Science Working Group. J Mol Diagn 1:3–16
55. U.S. Department of Energy Washington, D.C., Implementation guide for quality assurance programs for basic and applied research
56. Riegman PH, Morente MM, Betsou F, de Blasio P, Geary P; Marble Arch International Working Group on Biobanking for Biomedical Research (2008) Biobanking for better healthcare. Mol Oncol 2:213–222

57. Carter A, Betsou F, Clark BJ (2011) Quality management and accreditation of research tissue banks. Virchows Arch 458(2):247–248, author reply 249–50
58. Betsou F et al (2009) Human biospecimen research: experimental protocol and quality control tools. Cancer Epidemiol Biomarkers Prev 18(4):1017–1025
59. ISO 9000:2005 (2011) Quality management systems – Fundamentals and vocabulary. http://www.iso.org/iso/catalogue_detail?csnumber=42180
60. Centers for Disease Control and Prevention (CDC) 24/7 (2013) Saving lives. Protecting people. Saving money through prevention. Clinical Laboratory Improvement Amendments (CLIA). http://wwwn.cdc.gov/clia/
61. Pukkala E (2011) Nordic biological specimen bank cohorts as basis for studies of cancer causes and control: quality control tools for study cohorts with more than two million sample donors and 130,000 prospective cancers. Methods Mol Biol 675:61–112
62. Harris JR et al (2012) Toward a roadmap in global biobanking for health. Eur J Hum Genet 20(11):1105–1111
63. Centre for Cancer Genetic Epidemiology School of Clinical Medicine, C.U. iCOGS. 2013. http://ccge.medschl.cam.ac.uk/research/consortia/icogs/
64. Webster JD et al (2011) Quantifying histological features of cancer biospecimens for biobanking quality assurance using automated morphometric pattern recognition image analysis algorithms. J Biomol Tech 22(3):108–118
65. Solutions Ae (2013) Transforming the practice of Pathology
66. AOCS Study (2013) http://www.aocstudy.org/gp_about.asp
67. Office of the Australian Information Commission https://www.oaic.gov.au/privacy-law
68. Commission TE (2013) Data protection
69. The Wellcome Trust https://www.wellcome.ac.uk/funding/managing-grant/policy-and-position-statements (2013)
70. U.S. Dept of Health and Human Services. https://www.hhs.gov/hipaa
71. OEDC (2009) Guidelines on human biobanks and genetic research databases. https://www.oecd.org/sti/biotech/44054609.pdf
72. Schroder C et al (2011) Safeguarding donors' personal rights and biobank autonomy in biobank networks: the CRIP privacy regime. Cell Tissue Bank 12(3):233–240

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