State of Biobanking in the UK

Future Directions for Coordination

Draft for review 15 June 2021

UKCRC
TISSUE DIRECTORY AND COORDINATION CENTRE

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Vision

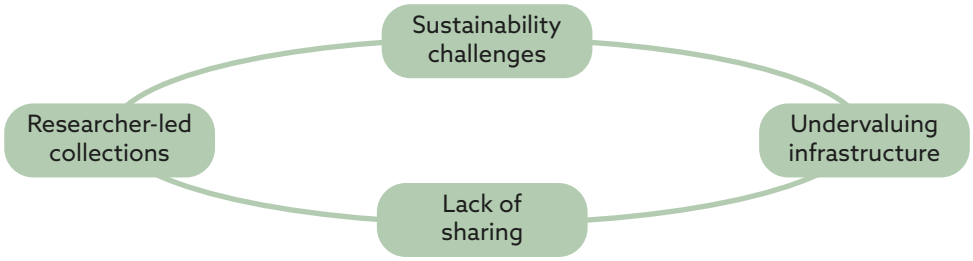
A data driven biobanking eco-system that:

- operates to open standards;
- embraces and drives open science;
- embeds public-led decision-making;
- re-uses infrastructure to drive sustainability; and
- focuses on simplifying and streamlining access procedures.

This vision will ensure the UK is at the forefront of global collaboration underpinned by world recognised infrastructure.

Challenge

Despite the United Kingdom (UK) being a world leader in clinical and medical research, it suffers the same challenge as every other nation: access to human samples is perceived to be slow, costly and lacking transparency. This creates a vicious circle of sustainability challenges, undervaluing of the infrastructure, promoting the perception that biobanks do not share, and the adoption of the default position for research-led collections.



Task

This discussion document sets out the current state of biobanking coordination in the UK from the perspective of the UKCRC Tissue Directory and Coordination Centre (TDCC). This document details current researchers' experience with accessing samples and data, key stakeholder opinion on biobanking coordination, and the lessons learned from TDCC. It then sets out the vision for future biobanking coordination in the UK.

EXECUTIVE SUMMARY

- Samples and data are the key building blocks from which so much research is undertaken. The ability to find and access both samples and data remains a challenge.
- UKCRC Tissue Directory and Coordination Centre (TDCC) was funded in 2014 to assist researchers in discovering samples and biobanks that could support their research, but it was not empowered to grant access to samples.
- According to TDCC research, researchers in the UK and EU opt for using a local resource or self-collection for sample access. This is due to the availability of data associated with the samples and the reduced governance burden for these methods (i.e. contracts to transfer samples are not needed).
- Self-collection then occurs out of lack of availability of existing suitable samples. When these collections are developed without forward planning, the cycle of limited access to samples continues. Without intervention encouraging legacy planning and sharing, this cycle will continue and is counter to efforts to promote open research.
- A review was undertaken by TDCC in 2020 which included 14 interviews with people and organisations representing interests in sample access and use, which identified from three themes that require action: transparency (public record of what is available), opportunity cost (better use of existing infrastructure), and research culture (sharing is not rewarded).
- It is time for a new vision of a new biobank eco-system that is data driven and seeks to make the most of existing infrastructure. This new eco-system will operate to open standards and be a passionate driver for open science and public-led decision-making.
- There is a need for the establishment of a new entity to deliver a governance framework to support the vision that is focused on utilising existing infrastructure to drive access to samples, underpinned by funders and regulators. This would deliver a national single entry point for delivering access to samples by providing researchers a single access point to the UK's rich and dynamic research infrastructure.
- The time for action is now as many of the relevant large research infrastructures are going through reviews or refunding.

Background

The provision of samples to support research is a vital foundation in the research and development landscape, particularly in translating fundamental research into new innovations in treatment, diagnosis and personalised medicine. Access to samples is a core requirement in both academic and commercial research. The disparity in access and lack of transparency, however, result in those with reliable sample access perceiving it as a competitive advantage for career or commercial progression.

There is undoubtedly significant investment worldwide in sample collection networks because of the direct reliance on samples in research and development. Internationally, however, access to samples is still cited as a barrier for research. The methods of coordination that have been deployed in the UK and beyond have not had transformational impact on these barriers. In this perceived competitive environment, the altruistic sharing of samples with others will always be challenging to pursue or encourage. A new vision is needed for the UK to become a sector leader, that is allied with the UK Government's *UK Research and Development Roadmap*.[1] Sample provision must be underpinned by transparency and FAIR principles,[2] such that the disparity of access is challenged and eventually becomes a non sequitur.

Research by TDCC[3] has found what influences the attitudes of researchers across the UK and the EU in sourcing from sample collections. It has also interviewed key stakeholders working in research infrastructure to understand the current barriers, options and desires for change for biobanking coordination in the UK.

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1 Department for Business, Energy & Industrial Strategy (2020) UK Research and Development Roadmap. URL: https://www.gov.uk/government/publications/uk-research-and-development-roadmap

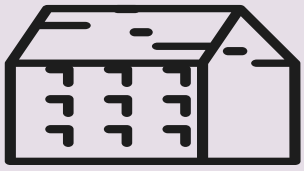
2 FAIR Principles. URL: https://www.go-fair.org/fair-principles

3 Lawrence, E., Sims, J., Gander, A., Garibaldi, J. M., Fuller, B., Davidson, B., & Quinlan, P. R. (2020). "The Barriers and Motivators to Using Human Tissues for Research: The Views of UK-Based Biomedical Researchers". *Biopreservation and Biobanking*. URL: https://doi.org/10.1089/bio.2019.0138

Researcher Attitudes

How do you currently source samples?

Local sample resource
39% UK researchers
48% EU researchers



Collect Samples
42% UK researchers
44% EU researchers

UK researchers:

The largest barrier to the use of samples in research was the "Lack of linked clinical data" with 42% (61/147) of respondents ranking it as either a significant or high barrier.

Surveys
A survey of 224 researchers in the UK and a survey of 290 researchers undertaken with BBMRI-ERIC (26 countries, including the UK) was used to establish the current attitudes of researchers for finding and gaining access to samples to support their research. The results demonstrate that researchers in the UK experience almost identical challenges to those across the EU. The motivations and barriers for use are largely the same.

The importance of locality
By far the most common method for current sample access is either via a local resource or self-collection. The factors driving this decision were the data available and the fact the supply of the samples were local. It is important to recognise, however, that when considering a new source for samples, locality was not seen as important. Researchers indicated that local sample collections are chosen for ease; however, they would also consider outside of their local network if the samples fulfilled their requirements. The fact that they would opt for self-collection over sample collections elsewhere is a consequence that they have unmet needs by the current sample ecosystem.

The importance of data
Data linkages were one of the main reasons for the selection of the current, and likewise a new, sample source. Importantly, however, the lack of available data was rated as the major barrier for the use of samples. It is clear that the eco-system is simply not able to supply what is required.

Governance
The structures for governance across Europe, both ethical framework and the material transfer agreements (MTAs), are seen as restrictive and a significant barrier. Therefore, whilst ethical approval is likely to be required regardless of local collection or accessing external bio-banks, clearly MTAs would not be required for local or self-collection routes.

Summary
The survey reveals compounding factors experienced within the domain. The lack of readily available clinical data, in combination with the perception of governance challenges, appear to be driving the behaviour for self-collection and local use. This was supported by the focus groups held after the surveys, which showed that due to the complexity of access externally it is beneficial to have a personal connection locally who can guide and assist the process.

Consequence of self-collection
The system indirectly encourages self-collection based on the per-

ceived challenges of accessing samples from external sources. There are, however, serious consequences of this approach that result in the proliferation of those perceptions. As a consequence, researchers collect locally and the practice becomes common practice and this further perpetuates that initial perception.

Incentives reproducing single-use samples
Researchers are usually required to invest their own time and money into securing samples, for example in obtaining ethics and recruiting participants. The investment in building collections makes sharing harder as samples represent the legacy of a project, rather than spare resource to be diverted elsewhere. The difficulty in accessing existing samples then increases their perceived value and therefore limits the likelihood of sharing.

Lack of planning
Sample collection is often funded at a research project level, usually without the infrastructure to share more widely. The collecting for one's own project becomes the most straightforward method if there is an absence of a suitable alternative. In reality, there is duplication of samples and infrastructure because the barrier to sample use is finding and accessing samples, not collecting them. Ultimately, sustainability of the domain is impossible due to the duplication. Research must both have the foresight to incorporate sample sharing in their original proposal by asking for additional resource to fund sample annotation, visibility and sharing at the end of the project. Neither of these are explicitly or implicitly encouraged within the current funding infrastructure.

UK researchers go abroad
Work undertaken by the Medicine's Discovery Catapult has highlighted the challenge experienced by UK Small and Medium-sized Enterprises (SMEs). There was a surprising result that 80% of UK SMEs found accessing samples from the UK to be difficult.[4] It was also found that the majority of those SMEs would then source samples from abroad. Sourcing sample from abroad is not beneficial in supporting our UK-based SME community, nor good for the sustainability of biobanks.

Summary
Self-collection is a consequence of the perceived challenge of accessing samples from external sources. The lack of sample availability then increases their value and disincentivises further sharing. This cycle will continue without intervention encouraging legacy planning and sharing. It is also clear that the UK based researchers face the same challenges as researchers based across the Europe and therefore highlighting that despite the world- leading infrastructure present in the UK, the challenge of access is still there. Opportunities to collaborate both in the UK and beyond (such as BBMRI-ERIC and ELIXIR) would be vital in breaking this cycle.

[4] BioIndustry Association and the Medicines Discovery Catapult. (2018) *State of the Discovery Nation and the role of the Medicines Discovery Catapult*. URL: https://s3.eu-west-1.amazonaws.com/media.newmd.catapult/wp-content/uploads/2018/01/16220811/MDC10529-Thought-Leader_v10_Interactive_v1.pdf

Review of Biobanking Coordination

In January 2021, TDCC conducted a review of "the state of biobanking coordination" with key opinion leaders. There were 14 interviews with people and organisations representing a range of interests in relation to sample access and use. These organisations were chosen based on their position vis-a-vis the biobanking domain and represented researchers, research funders, patient groups, government regulators, clinical trial groups and biopharmaceutical companies. Representatives were asked a series of questions to elicit reflections on what is working well in biobanking, as well as potential areas of focus for future improvement.

The discussions from each group were analysed to identify themes of work to further improve biobanking coordination. The themes identified included transparency, opportunity costs, and research culture. All the participants attended a 'round table' event to agree and comment on these initial findings. It was agreed these were representative of the conversations and that the next step should be the generation of the vision document.

Who we spoke to

- Adaptimmune
- BC Platforms
- Glasgow University
- Health Research Authority (HRA)
- Human Tissue Authority (HTA)
- IQVIA
- Medical Research Council (MRC)
- Medicines Discovery Catapult
- National Institute for Health Research (NIHR)
- Our Future Health
- Royal College of Pathologists
- UseMyData

Themes

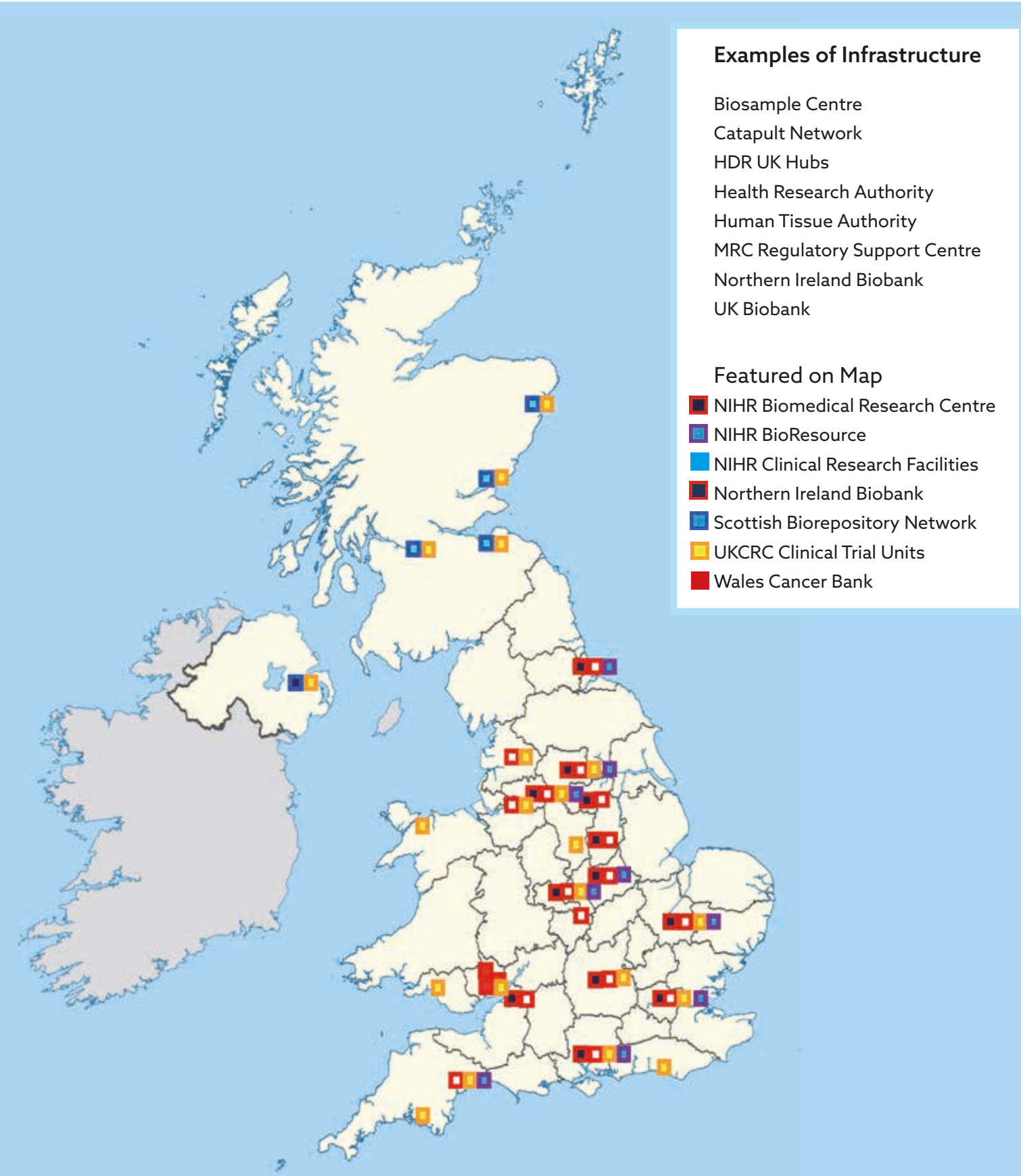
Transparency
The interviews revealed a consistent concern that the current methods of finding, accessing and using samples from biobanks was lacking transparency. This was particularly the case in relation to sample access decision-making. It was stated that although some sample holders may state open access, that this was rarely the case. Access requests would be judged on the merits of the application and the decision-making process for access was not available for scrutiny. It is also not currently an ethical assessment criterion for research tissue banks to have their access processes or the constitution of their access committees examined by regulators. The consequence is that the uncertainty of the process and criteria involved in accessing existing sample collections further drives the additional collection of samples, and subsequent inaction to sharing.

Opportunity Costs
Significant investment has been made in the UK to develop world-leading academic and commercial research infrastructures. However, in the interviews it was felt that there are examples where research council and charitable investments could be optimised by more comprehensive coordination. Of particular note was that the UK clinical trials infrastructure was widely praised as a key asset. However, there was also a desire for clinical trials and the associated infrastructures underpinning clinical trials to be better used for the collection of bespoke samples for research. Consent was also raised as a lost opportunity. Usually, consent is defined at the level of a project rather than embedding provisions for cross-project or subsequent re-use of samples. Each project creating new consent forms adds cost to the research programmes and reduces the ability to share and link samples and data later.

Culture
The focus groups highlighted the importance of research culture in influencing sample access. Whilst most participants were frustrated with the fact that samples were not more readily available to other researchers, there was also agreement that the research eco-system rewarded the wrong behaviour. It was felt that it was unrealistic to expect samples to be shared to potential rival groups given that biobanks are often a consequence of a research project, and the effort and financial input required from the researchers to develop the collection. It was also commented that directly challenging the wider eco-system would not be the right approach. Instead, culture may be changed through leading by example, building transparency and utilising the opportunity costs to influence behaviour over time.

World-leading Infrastructure

The UK has an impressive arrangement of infrastructure to support research. The following list is not exhaustive, but provides examples to the breadth and depth of support and resources available.



Lessons learned from TDCC

The UKCRC Tissue Directory and Coordination Centre (TDCC) was built on the widely held desire for biobanking coordination in the UK. The UKCRC Experimental Medicine Group produced a Vision for Human Tissue Resources in 2011, for both free-standing sample collections and collections as a result of discrete studies. They declared,

> *Funders aim to maximise the value of human tissue samples and resources while minimising duplication of effort. This requires better characterisation of tissue samples, asking for generic consent, and increased linkage to accurate clinical data. Sample collections must then be made more easily discoverable and accessible for use in high quality, ethical research.*

TDCC was created at the end of 2014 to fulfil part of the Funder's Vision. It is home to the Tissue Directory,[5] the publicly accessible directory of sample collections in the UK. This Directory was intended to drive biobanking coordination by harmonising how collections are described and made visible to researchers. This was so that researchers could find and use suitable samples external to their local networks.

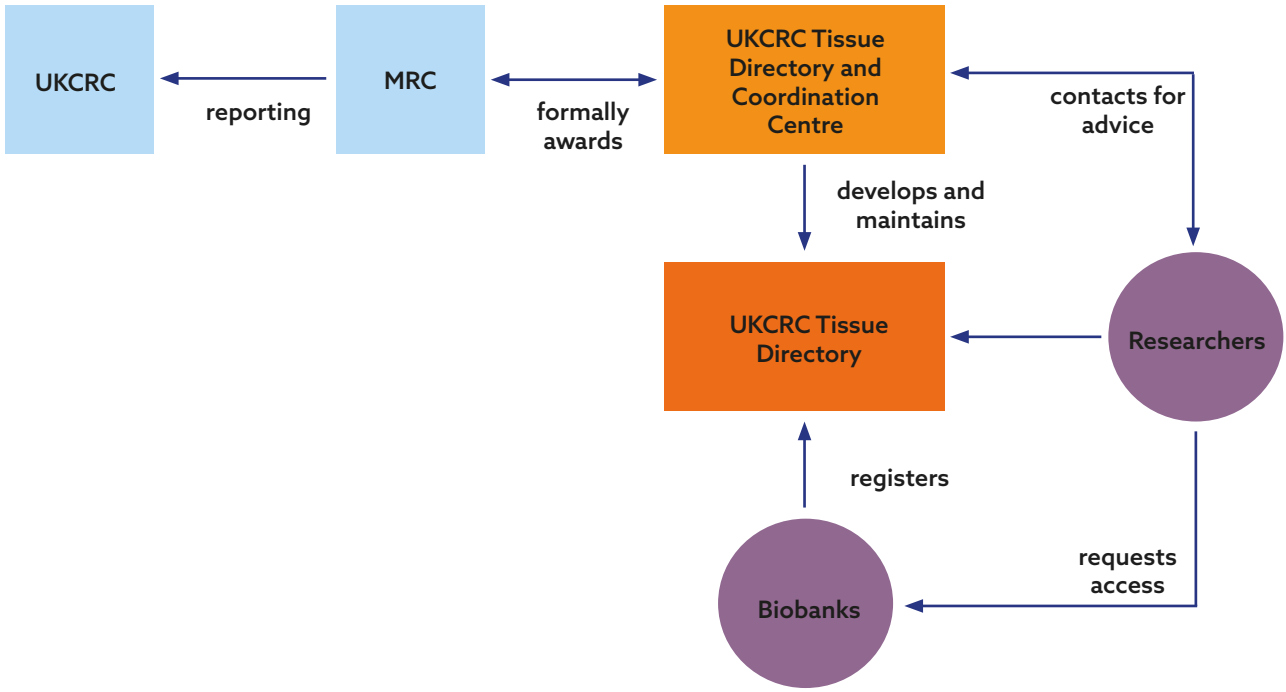
The Directory was the first of its kind as it is cross-disease and had a remit across all sample collections. The Directory lists over 225 sample resources (biobanks, biorepositories, clinical trials and cohort studies) which can collect samples. Researchers can find samples affected by particular diseases for their research, as an alternative to creating new collections by asking patients to donate samples.

TDCC's research on researcher's views towards sample access has highlighted that it is important to have widely accessible information of available samples. However, sample visibility does not necessarily translate to accessibility, as access is ultimately up to sample custodians or the committees in place to assess access applications.

TDCC was not positioned or empowered to tackle challenges in accessing samples. It has succeeded in its primary role, a body to make samples visible. It's success as a coordination centre to change the culture of sample access,

[5] UKCRC Tissue Directory and Coordination Centre. URL: https://directory.biobankinguk.org

Current organisation of the Tissue Directory and Coordination Centre



however, has been limited by its role as a retrospective coordinator: initiating communication with projects and resources after funding, consent and ethics are in place.

TDCC will not continue in its current form beyond 2021. If ended completely, the progress made so far would be lost. There would be no central catalogue of sample collections, no organisation to facilitate consensus-building in community standards, and further disincentives to open research. An initiative which is empowered to provide up-front coordination is needed to drive culture change in sample access, and connect the disparate parts of sample infrastructure. It should build on TDCC's work to further improve biobanking coordination.

Key developments in coordination:

- Registration is a condition of favourable ethical permission
- 65,000 users of the website and directory from 2015
- 4000 access requests
- 248 biobanks registered

The 2030 Vision

The Vision
A data driven biobanking eco-system that:

- *operates to open standards;*
- *embraces and drives open science;*
- *embeds public-led decision-making;*
- *re-uses infrastructure to drive sustainability; and*
- *focuses on simplifying and streamlining access procedures.*

The UK needs, and has the capability for, a world-leading sample acquisition infrastructure. The UK is seen as the gold-standard in research governance, notably with the involvement of patients and the public in decision-making processes. The component parts of the research infrastructure are well-established resources, however, there is no one central body which links them together.

A hub which facilitates a coalescing service would transform the UK landscape for academic and commercial research. It would result in a system with clearer routes to sample acquisition and management, even if from the inside the parts of the infrastructure are administered by different organisations. The approach would make the UK the international hub for sample-based research, as it is already for clinical trials and translational research. This would increase transparency and build on existing and emerging strengths within the sector, irrespective of scale, to ensure that public investment is maximised.

There is a rare window of opportunity to align, optimise and enable this collaborative network as TDCC is under review, and the Biomedical Research Centres and the Clinical Research Facilities are undergoing a renewal process. The Health Data Research UK Data Hub programmes are now maturing, are expected to be sustained in the next year, and will be joined with a new Population Research UK hub in 2021.

We have outlined two areas of development for the future of biobanking based on the experience of TDCC and the perspectives gathered in our review:

- establish a new governance framework; and
- funder and regulator alignment.

Establish a new governance framework

A new (or repurposed) entity will be required to coordinate, create and manage the implementation of a single governance framework to enable sample and data access. The coordination centre will be be a beacon of excellence, acting as an umbrella organisation to develop and implement best practice. The lessons from TDCC and previous coordination efforts should be incorporated to ensure this coordination centre acts as a collaborative of many organisations supporting the delivery of the vision, rather than a single entity that will achieve the vision in isolation.

What is needed:

- Coordination of access to samples across the UK.
    - Develop a single cost recovery model.
    - Harmonise consent, such that is comparable if not identical across locations.
    - Develop agreements with existing infrastructures that collect samples under this governance framework.
    - Build relationships with key data partners (HDR UK, NHS-D/X) to ensure data linkage is enabled
- Work across industry and academia, focused on the appropriate use of samples for research that follows the instruction of consent.
- Bring patients and public into the decision-making process.
- Develop a sustainable model for the entity.

The coordination centre will form relationships with existing national infrastructure to capitalise on existing investment in UK research landscape that could be utilised for sample collection and data linkage. The coordination centre would not seek to hold samples or data directly, but it would provide a knowledge transfer and governance umbrella framework that would result in access, through application, to samples and data from partners.

Data Linkage

The proposed coordination centre would seek links with Health Data Research UK (HDR UK) to ensure the largest blocker (lack of clinical data) is also tackled in partnership. HDR UK has an exciting programme of Digital Innovation Hubs which works with the users of data to provide insight and access to datasets managed and controlled by their partners. This HDR UK Innovation Hub Programme has demonstrated success in providing a single access point to datasets which may not have been known outside of their local networks. These existing data hubs could offer a natural interaction point for the new umbrella hub to deliver a data driven biobanking vision, and the HDR UK Hub Programme could equally act as a framework to instantiated the new coordinating centre.

Historical collections vs Prospective Collections
TDCC has been working to form a Biobank Alliance to unpick the governance hurdles to implement a single application process across organisations from existing permissions. This can be challenging to unpick potentially decades of consenting and access practices in historical collections. The new governance framework would initially be constructed to assist in providing researchers with a single location to request new samples to be collected from the partner infrastructures. Legacy samples will be brought inline, if possible, if there is perceived value and equally if the consent is enabling for the required data linkage. Aside from sample access, the coordination centre would also work to develop baseline models for cost recovery to facilitate sample reuse. It would seek to develop agreements with existing sample collection infrastructure to ensure that the commitment is ongoing.

Public involvement and engagement
Research should be held to account by the public who funds it. The coordination centre will seek to provide and promote opportunities for public involvement and engagement in the samples and data research ecosystem. TDCC has provided a central information point for samples-based research so far, however for the purpose of research use rather than public engagement or awareness raising. The public should be involved in the research decision-making process, not just on the local access level but throughout all levels of the biobanking ecosystem. Joining up processes and systems between organisations allows the transparency needed for the public to understand where and how they can be involved in decision-making. The coordination centre will need the public to help drive open research culture change and make the resources available for it to meaningfully work.

Funder and regulator alignment

UKRI has called for the identification of opportunities for increasing interconnectivity, future research and innovation capabilities and priorities.[6] Better utilisation of existing sample infrastructures across funders would be a vital component to respond to this call to action.

The new coordination centre can assist in pro-actively identifying opportunities for such alignment and speak effectively to the public, government organisations and national funders. There is an opportunity to bring the major UK research infrastructures under a common vision for sample access, such as through the renewal processes for HDR UK and the Biomedical Research Centres. At the same time, working with regulators can ensure the identified governance barriers (real or perceived) can be removed.

What is needed:

- Commitment to work with the coordination centre to align core research infrastructures under a common vision to maximise value.
- A clear roadmap from regulators on working with the coordination centre to enable access across infrastructures to manage legacy permissions to align with the UK government research roadmap.
- A joint policy across funders to strongly promote the use of existing research infrastructure where sample or data are likely to be retained beyond the initial funding period.
- A focus from regulators on transparency of access to research tissue banks.

It is clear the opportunity costs can only be addressed with greater coordination with funders from across the medical research domain. The coordinating centre will work pro-actively with funders and regulators to reduce the opportunity cost and to ensure existing investments can be fully utilised. The alignment and realisation of a common sample access vision among research infrastructures will offer researchers a credible alternative to self-collection and further fragmentation.

Now is the time to create a single entity to coordinate access to samples and linked data for the benefit of the wider research eco-system. A clear motivation for change will be through strategic investment. As HDR UK have demonstrated, the use of funding to drive alignment can bring powerful benefits. This unique opportunity should not be missed.

Governance and ethical approval are still perceived to be a major disruptive barrier in the use of samples. The regulators provide a key governance framework but also set the standards for the community to operate. It will be important for regulators and support services, such as the MRC Regulatory

[1] Department for Business, Energy & Industrial Strategy (2020) UK Research and Development Roadmap. URL: https://www.gov.uk/government/publications/uk-research-and-development-roadmap

Support Centre, to work closely with the new coordination centre. This will assist garnering public-wide support, busting governance myths and ensuring the relevant permissions are granted to projects.

It can often be the case that a project designed as a resource for wider use has inappropriate or disproportionate ethical permissions. Also, those that were designed to be a single collection have permissions which maybe are not required. The coordination centre can help in the creation of national standard process that can be adopted locally, to maintain the UK as the gold-standard in governance, whilst providing efficient and transparent access to samples for researchers.

Conclusion

This document has set out to describe the challenge to sample access in the UK in order to realise a new vision. TDCC hopes to build support with the key research infrastructures listed and to work with funders to understand the ways in which the vision can be implemented

The vision builds on the success of TDCC with the aim of delivering a real capability step-change in the access to samples and data. This has been based on significant research on researchers and focus groups to ensure the voice of the users is heard and represented.

- Transparency will be addressed by setting a new level of best practice for decision making and public involvement in decision making.
- Transparency will be addressed by maintaining the public record and the Tissue Directory.
- Opportunity cost will be pro-actively managed with funders so that new investments in UK infrastructure aligns with the vision.
- Culture change will be tackled by leading by example.
- Culture change will be achieved by acting as a beacon which will be open to all to join if they agree to the new way of working.

The consequence is an exciting opportunity to bring significant change to an area that has faced consistent challenge for researchers. The time is now to act and make the change.

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