Final Report

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Project	WAHTN-MRFF Rapid Applied Research Translation Program - Biobanks	**Period covered**	1 August 2018 to 7 December 2018
Forecast closure date	15/12/2018		

A. Activity Description

Careful management of biospecimen for current and future research is fundamental to high quality and reproducible research resulting in medical advances. There is a need in WA to establish a harmonised sample collection, storage, curation and management system that will allow ethically acceptable standardisation across cohorts and registries and avoid duplication of effort and investment.

The aim of the project is to develop recommendations for national guidelines and piloting infrastructure for a scalable, shared, standardised data repository of clinical and research genomics resource facility in WA. The project, which can be scaled to national activity, will produce an international scan of biobank resources, facilities ethics and economics across Australia, the UK and Japan.

B. Progress Summary

- A questionnaire (Appendix 1) was sent out to a number of stakeholders in WA (Appendix 1A) to gather information and feedback on the establishment of a centralised biobank in WA, with follow-up interviews with individuals to clarify and understand the data and specimen banking requirements across different studies/biobanks in WA.
- A stakeholder engagement workshop was held with the aim of developing working groups to further advance the discussion points around Governance, Ethics, Quality Assurance, Data management, Infrastructure and Funding.

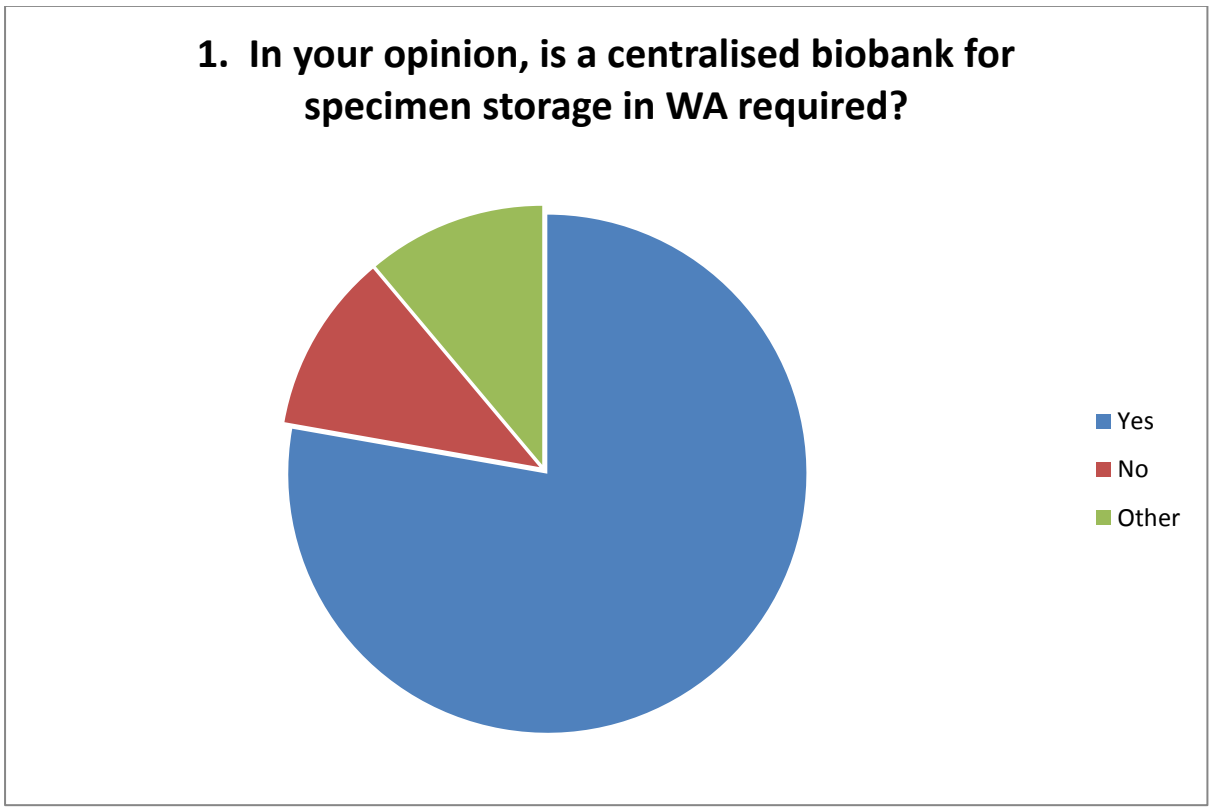
- **Summarise findings to understand the data and specimen banking requirements across different studies/biobanks**

A questionnaire (*Appendix 1*) was developed and sent to a number of WA stakeholders in order to understand the needs and requirements for a centralised biobank management facility. The aims for the questionnaire were:

a. to capture the heterogeneity of biobanking activities within WA
b. to increase understanding of the organization of biobanking within WA
c. to compare institutional and funding arrangements as well as specific specimen requirements in existing biobanks in order to provide insights into the costs and benefits associated with different biobanks

Although the completion rate was low, responses were received from all the major biobank stakeholders and some hospital representatives. In summary, over 75% of respondents agreed that there is a need to establish a centralised biobank in WA. Almost all respondents would like to see a standardised and integrated system to enable investigators to locate, share and link data while adhering to national and international ethical and legal guidelines. Most respondents would like to have a database with functions to identify sample storage, processing, aliquots and freeze thaw records. A list of current specimen stored in various biobanks is also obtained (detailed summary in *Appendix* 2). Interviews with individuals were also carried out to understand the specific data and specimen banking requirements across different studies/biobanks in WA.

Overview of Questionnaire Survey Results



2. What functions would you like to see in place across WA biobanks (e.g sample collection, handling, processing, storage)?

All of the above. DNA extraction. PBMC extraction.

As most bio-banking including tissue registries are held in private facilities and even interstate or overseas in the case of Clinical Trials, there needs to be a discussion with key stakeholders regarding capability to adhere to like standards and protocols. Many international protocols are governed by stringent European standards and so there also needs to be benchmarking with best practice standards globally to ensure WA does not "reinvent the wheel".

yes - sample collection, handling, processing, storage
BUT how will this be integrated with patient identification and consenting?

Yes all of the above

SOPs for sample collection which provide samples suitable for multiple purposes - i.e. some for potential NGS, some suitable for single cell sequencing perhaps, concurrent blood for serum/PBMC would be helpful. Long term storage and a transparent access process.

Ownership of the specimens
Adequate Freezer Storage
Back up storage space
Security system
Standardised freezer care and maintanence

A well standardized and integrated system to enable investigators locate and share samples and the associated data, while adhering to national and international ethical and legal requirements,

is critical for obtaining high quality and meaningful research, particularly in the field of rare diseases.

If facilities can allow widespread sample collection then would If facilities can allow widespread sample collection then would be desirable, but not essential, the ability to offer handling and processing would be good, storage, curation and ability to manage the biobank and provide samples for future research would be essential consideration for mirroring of biobank to ensure that in case of infrastructure failure that samples are not lost

All of the above: sample collection, handling, processing and storage

3. What database functions/IT requirements for specimen management would you like to see in place across WA and elsewhere?

A biorepository database including sample location, number of aliquots, number of freeze/thaws etc

Again, given privacy and protocol variations and differing governance requirements, this needs to be a discussion point at a forum, noting again European standards already exist around ICT and research governance. There should also be consultation with authorities in this area such as Dr Nik Zeps, formerly Director for Research at SJGHC who set up the bio banks there for tumour tissue. He is now director of research at Epworth in Melbourne.

It all depends on consent - at least we could have database for sample storage, processing, aliquots and number of times defrosted.

Unsure

Best would be import from routine clinical information, ideally data linkage with hospitals, PBS, MBS. Expecting clinicians to input data in the context of a busy clinical load is a recipe for missing information - having run a brain cancer biobank previously; this is a significant additional impost and just cannot fit into the clinical workload in the context of competing priorities such as patient care.

Data storage systems

Biobanks (BB) are gradually becoming more recognised as invaluable tools to drive basic and translational research for RDs. BBs collect and store biological specimens with matched clinical data and patient metadata in an organised system, distributing samples and data to the scientific community, enabling ‘omics studies. This is especially important considering drug innovation for RDs has, in recent years, become progressively focused on ‘omics-type research, and that more than 80% of RDs have a genetic component. RDs have recently been referred to as “fundamental diseases”, highlighting their unique capacity in providing opportunities to investigate the “extremes of human pathology”. For example, research of LDL-receptors in familial hypercholesterolemia, a rare disease, led to the discovery of statins, a drug therapy that is now also routinely used to prevent heart disease.

Ability to assess what samples are available and how they were collected
ability to note what volume or amount of samples are available
records or staorge, freeze-thaw and other handling would be essential

Database generation capabilities, which could store meta-data, and manage external access to the data

4. Have you seen other biobanks and database that you like and have functions that you require? If yes, please name these systems and features.

Bendat Centre biobanks under Prof Cameron Platell at SJGHC - based at Subiaco.

Buseelton Health Survey/BHAS

Brain Cancer Biobanking Australia had a robust process for developing data fields - this is an overarching virtual biobank but the data fields are categorised as Essential, Preferred, and Comprehensive. Clinicians and scientists reached consensus on categorisation.

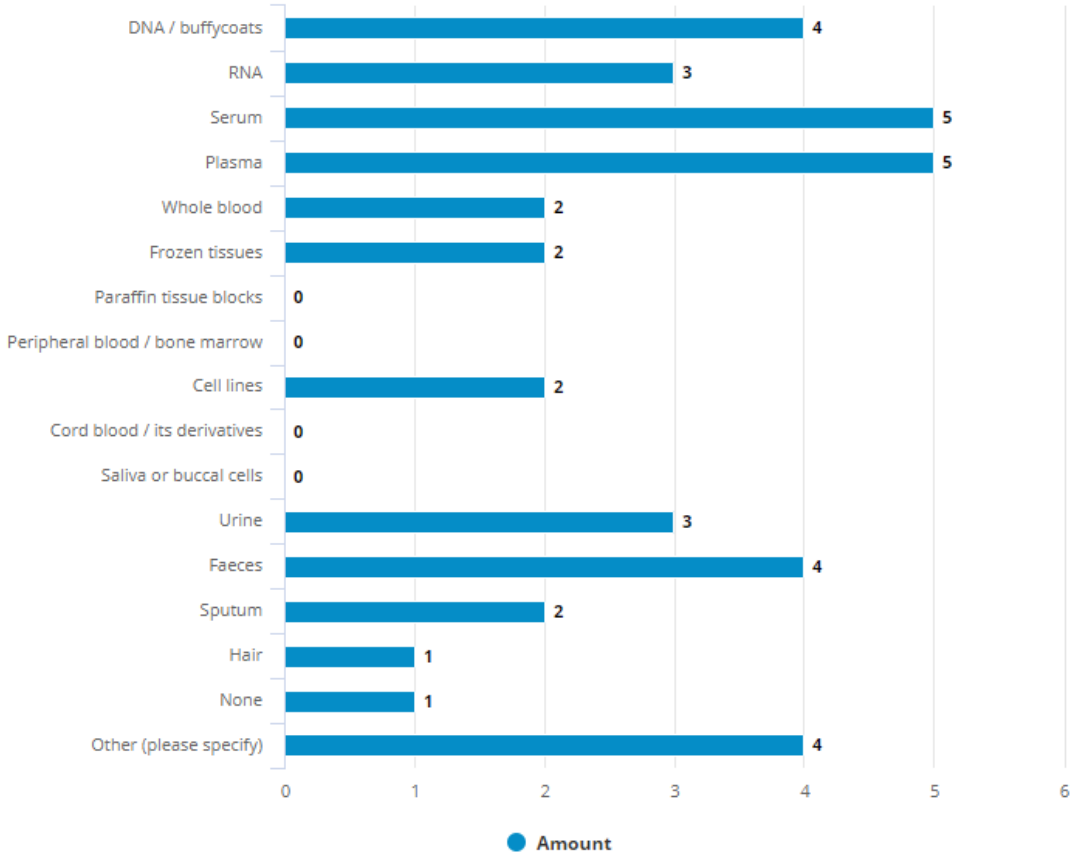
UK BIOBANK
China Biobank
The Eurobiobank Network
Telethon Network of Genetic Biobanks
The European ARPKD registry
Eyegene
European Management Platform for Childhood
The CREST biorepository
Italian Huntington Disease patients - data and tissue bank
The Dutch Lymphangioleiomyomatosis (LAM) registry
The Australian Rett Syndrome Database
The InterRett Database
The Rare Disease Bank of Japan: establishment, current status and future challenges

This question seems to allow only 1 choice. We store urine, plasma, serum, exhaled breath condensates. We collaborate with others that collect epithelial cells from cohort we engage with and so also have an interest in cell lines

Raine Study - they have it working very well now

5. Do you store biospecimens? If so, which of the following biospecimens do you store?

Number of responses: 9



6. If you store biospecimens, what number of specimens and aliquots are currently in storage?

100's

>20,000

>1,000

1000+ samples from patients with glioma.

> 4000 aliquotes (2 ml cryotubes)

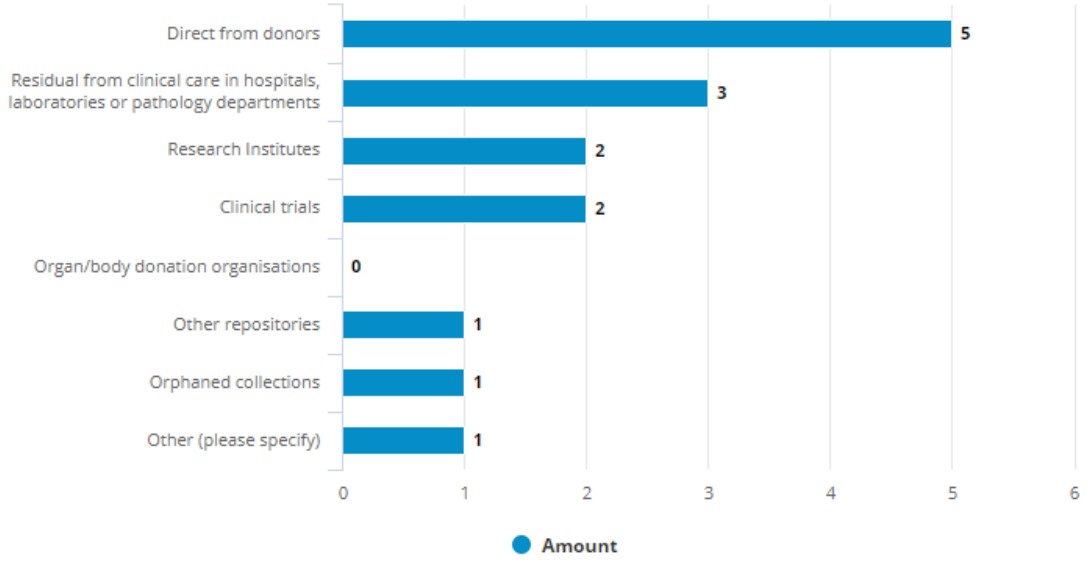
200

Multiple samples from 1000+ participants, across longitudinal samples

approx 5000

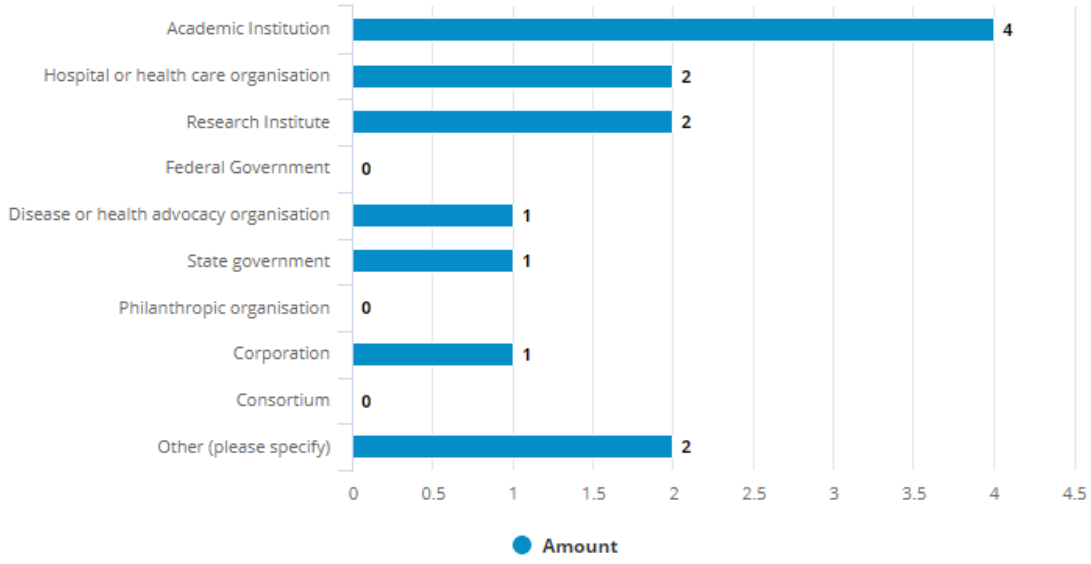
7. Acquisition of specimens

Number of responses: 8



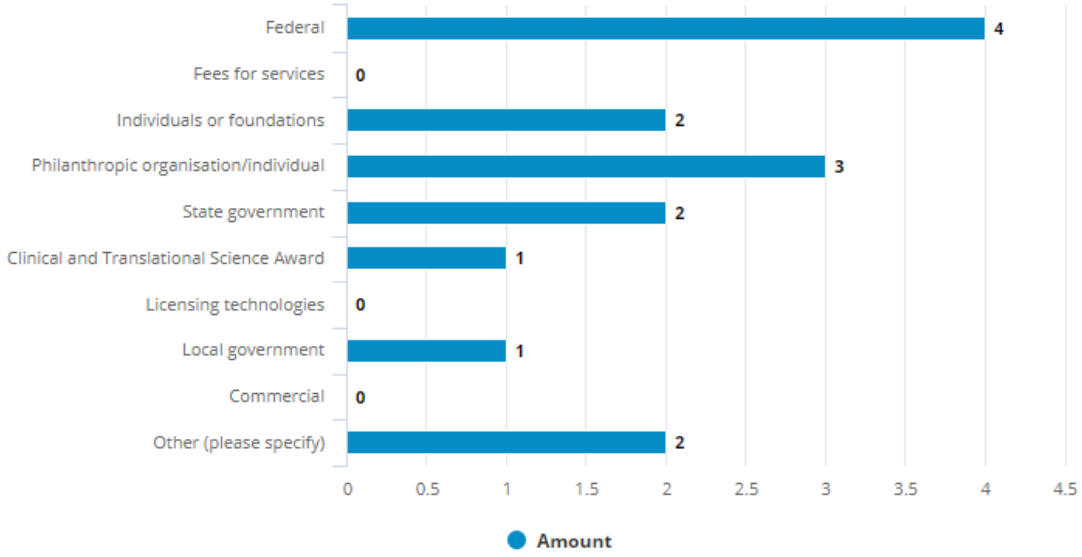
8. Who does the collection belong to?

Number of responses: 8



9. What has been your funding source in past 5 years?

Number of responses: 7



- **A stakeholder engagement workshop to develop working groups.**

To further engaged and seek input from all the stakeholders in WA, an engagement workshop was held in October. Over 50 individuals representing the all four Universities, major hospitals as well as leading research institutes participated in the workshop. Further information on the workshop are summarised in appendix 2A-2C and can be found on https://www.wahtn.org/bio-bank-workshop/

Progress against Performance Indicators

Performance against the performance indicators in Item B3

- **National and international comparisons**

The 6 biobanks and networks chosen for this review represent a geographically diverse set of organizations with different approaches to collection and storage. Table 1 summarizes the characteristics for the 6 biobanks from countries listed in Item B3 under outputs.

Name	Scope	Collection	Storage	Biospecimens
Australasian Biospecimen Network	Cancer	General, (project-driven on request)	Federated	Tissue, blood, DNA, RNA, tissue microarrays, cell lines
NSW Statewide Biobank	Various	General	Centralised	Tissue, blood, DNA, cell line
UK Biobank	Various	General	Centralised	Blood, urine, DNA
EuroBioBank	Rare diseases	General	Federated	Tissue, DNA, cells
Cooperative Human Tissue Network (USA)	Cancer	Project-driven	Federated	Tissue, blood, tissue microarrays
Tohoku Medical Mega Bank Organisation	Populational based	General	Federated	Tissue, DNA, blood, cells, urine, breast milk, saliva

Australian biobanks are beginning to self-organise into local and national networks and facilities. Examples include the Australasian Biospecimen Network association (http://abna.org.au/) and the recent establishment of the NSW Health Statewide Biobank (http://biobank.health.nsw.gov.au/). Paediatric cancer biobanks in Sydney have also networked under a common governance framework to form the Sydney Children's Tumour Bank Network (https://www.schn.health.nsw.gov.au/). At a national level, Brain Cancer Biobanking Australia (BCBA, http://www.bcba.org.au/) was established under the umbrella of the Cooperative Trials Group for Neuro-Oncology (COGNO) with the aim to accelerating brain cancer research and the translation of that research into improved outcomes in patient care. BCBA is a virtual biobank hub established to provide researchers easy access to the amount, quality and type of tissue and associated data they need to accelerate both paediatric and adult translational brain cancer research. It is committed to supporting research performed by clinicians and scientists in the brain cancer fields. One of their aims is to leverage and harmonise existing resources in order to increase the quantity and quality of available specimens.

Countries such as Canada (http://www.ctrnet.ca/), France (http://www.biobanques.eu/), UK (http://www.ukbiobank.ac.uk/), Spain

(http://www.redbiobancos.es/Plataforma.aspx?i=100&p=158) and Japan (https://biobankjp.org/cohort_3rd/english/ ;https://www.megabank.tohoku.ac.jp/english/) have all invested in national biobanking programmes which allow for the development of networks. Biobanks across Europe are also benefiting from major infrastructure initiatives.

EuroBioBank is a unique network of biobanks consisting of 25 rare disease biobanks located in 11 countries. It stores and distributes quality DNA, cell and tissue samples to scientists to conduct research into rare diseases.

UK Biobank is a population-based initiative that banks biospecimens from British participants for broad research purposes. It is funded by the UK government and charitable organizations. When the biospecimens become available to investigators, a cost-recovery plan will be employed to defray the costs of obtaining the samples and accompanying data as well as any preparation or analysis requirements requested by the accessing researchers.

Tohoku Medical Megabank Organisation was founded to establish an advanced medical system to foster the reconstruction from the Great East Japan Earthquake. It aims to develop a biobank that combines medical and genome data which will attract more medical practitioners to the area.

Australia would be in a stronger position to interact with these initiatives if we could also feature a coherent, organised biobanking sector through which international initiatives could be efficiently translated.

Different biobanks around the world have different funding sources and cost charge per samples. The cost ranges from only charging for transportation cost, to a fee to cover collection and handling, to fully borne by the requesting researcher. Table 2 summarises the 6 biobanks, their funding sources and price per sample.

Table 2. Funding sources and price per samples for 6 biobanks

Name	*Funding Sources*	*Price per Sample*
Australasian Biospecimen Network (Australia)	**Government (Australia) and public/advocacy**	**Available upon request**
NSW Statewide Biobank	**Government (Australia), commercial, and public/advocacy**	**Varies depending on for profit or not for profit; Partial cost recovery:**
		A$12.5 for tissue processing
		A$16.5 for DNA extraction and QC
		A$25 per blood collection
Tohoku Medical Megabank Organisation	**Government (Japan)**	**Partial cost recovery**
Cooperative Human Tissue Network (USA)	**Government (USA)**	**Investigators pay a nominal processing fee for samples in addition to shipping. Slides and blocks to accompany frozen or fresh tissue specimens may be available for an additional fee.**
EuroBioBank	**Government (European Commission) and charitable**	**Varies by participating bank: processing and shipping fees apply**
UK Biobank	**Government (UK) and charitable funding**	**Partial cost recovery**

- **Strategy for implementation and funding of State wide resource; potentially scalable nationally.**

A stakeholder engagement workshop was held in October 2018. The aims of the workshop are:

1. to identify common biobank resources required for diagnostics and research work in WA.
2. to invite users to express their views in developing a centralise biobanking facility in WA and to address the needs and potential problems associated with a national biobank resource
3. to provide an overview of the opportunities for biobank users in WA
4. to develop a working group with expertise in (i) Governance, (ii) Ethics, (iii) Quality standards, (iv) IT and (v) Expert advice to government and funders.

Following the stakeholder engagement workshop, the following approaches have been or are being actioned.

1. Initiate actions by a working group small enough to efficiently move these forward with set template working group reporting *(Appendix 3 and 4*)•
2. Hold user group meetings to agree on practical issues and move things forward. •
3. Involve existing biobanks and ongoing high-throughput research in order to• harmonise standards and procedures at a national level and so that efforts will not be duplicated but built upon. •

Milestones and timeline for steps required for implementation

Milestones : October 2018 - Sept 2019

	Milestone	Oct-18	Nov-18	Dec-18	Jan-19	Feb-19	Mar-19	Apr-19	May-19	Jun-19	Jul-19	Aug-19	Sep-19
	Project planning and workshop												
Stage 1	Establish project working groups												
	Recruit working group leads												
	Develop engagement plan												
	Consultation and engagement												
	Develop scoping/discussion paper												
	Incorporate feedback												
	Finalise paper and obtain consensus to proceed to Stage 2												
Stage 2	Establish a governance group												
	Identify and recruit project leads												
	Implement stakeholder engagement												
	First Governance group meeting												
Stage 3	Implementation according to priorities												

Figure 1. Milestones for steps required for implementation

Summary

There is no doubt that WA needs to establish a harmonisation sample collection, storage, curation and management system that will allow ethically acceptable standardisation across cohorts and registries.

The last National Research Infrastructure Roadmap was released in 2016, with two of nine focus areas relevant to biobanking: 'Therapeutic Development' and 'Complex Biology'. The Government response to the roadmap released in May 2018 have identified funding allocated to (1) scope the investment needed to maximise the broad range of biobanks across Australia, as well as funding to (2) improve underlying infrastructure to link more health and population data collections (appendix 5).

In summary, this report summarised the findings gathered through (1) questionnaire, (2) interviews with individuals and (3) stakeholder engagement workshop.

Apart from the biobanks and networks described, a number of cohort studies as well as researchers were interviewed in order to understand their economic and governance models. Although generally successful, some challenges are worth noting to inform new initiatives.

- **Financial issues:**

Biobanking is an expensive activity requiring permanent space and dedicated staff for collection and processing of samples. Experience from the WA DNA bank has shown that the costs of establishing and maintaining a biobank are large and it requires continuous funding for infrastructure maintenance and general operation cost. A full cost recovery model is not feasible as it is generally not supported by users.

- **Access and custodianship to the long-term sustainability of a biobank.**

A governance plan should be established prior to the inception of a centralised specimen and data bank with guidance from stakeholders and/or an independent advisory board, to identify who is the custodian of biospecimens, with detailed protocol to ensure the long term quality of samples and the integrity of their associated data. The plan should define principles for protecting the privacy of human research participants and the confidentiality of their associated data, access to biospecimens and data, management of discontinuation of participation in research, and potential administrative changes during the term of the project.

- **Public engagement to assure the public that the specimens are being used in an ethical and productive manner**

In the past, research participants have not always been advised on research outcomes and have had to rely on their own ability to gather news reports or research publications in order to track new findings. This is a practice that may be out of reach for many lay or older participants. Today, however, a variety of methods are available to disseminate aggregate research findings especially through the social media. However, this requires time, expertise, and funding and should be included in the planning of the biobank.