

Submission

2016 National Research Infrastructure Roadmap Capability Issues Paper

Name	A/Prof Jennifer Byrne
Title/role	Head, Children's Cancer Research Unit
Organisation	Kids Research Institute, The Children's Hospital at Westmead, NSW

Introduction

Thank you for the opportunity to comment on the 2016 National Research Infrastructure Roadmap Capability Issues Paper. This submission is supported by the following organisations/stakeholders:

- NSW Health Pathology (Professor Roger Wilson, Chief Pathologist; Ms Jane Carpenter, Program Manager, Biobanking Services)
- Australian and New Zealand Children's Haematology/Oncology Group (Dr Chris Fraser, Chair)
- Brain Cancer Biobanking Australia (Professor Anna Nowak, Co-Chair; Professor Michael Besser, Co-Chair; Ms Robyn Leonard, Founder; Dr Mythily Mariasegaram, Project Officer)
- Sydney Children's Tumour Bank Network (Ms Amanda Rush, Chair)
- Children's Hospital at Westmead Tumour Bank, NSW (A/Prof Daniel Catchpoole)
- Monash Children's Cancer BioBank, VIC (Dr Peter Downie)
- Telethon Kids Institute, WA (Dr Nick Gottardo)
- Women and Children's Hospital, SA (Dr Maria Kirby)
- Children's Cancer Centre Tissue Bank, Royal Children's Hospital, Murdoch Children's Research Institute, VIC (Prof Richard Saffery, Dr Françoise Mechinaud, Dr Louise Ludlow)
- Children's Cancer Institute Tumour Bank, NSW (Dr Jamie Fletcher, A/Prof Claire Wakefield)
- Queensland Children's Tumour Bank (University of Queensland) and the Lady Cilento Children's Hospital, Qld (Dr Andrew Moore)
- Cancer Society Tissue Bank, Christchurch NZ (Dr Siobhan Cross)

This submission concerns the activity of biobanking, and endorses the discussion paper's focus upon the need for integration and consolidation of biobanking across Australia (page 16, section 5.2.4).

Biobanking is a key research infrastructure capability that is essential for Health and Medical Sciences and it is an investment in the overall health of Australians. Biobanks have a pivotal role in accelerating translational research and improving the prevention, diagnosis, treatment and ongoing management of diseases. The demand for well annotated biospecimens and associated data is growing due to the advances in technologies and tools that can improve patient care and facilitate precision medicine. Australia needs to invest in a national framework for biobanking to drive translational research that will lead to improved health outcomes for all Australians. This will also facilitate and increase international collaborations and Australia's participation in large international health and medical studies.

This submission proposes that the voluntary biobank certification scheme that is being delivered in NSW by NSW Health Pathology, could be adopted Australia-wide to provide a basis for national

biobank networking and oversight. A national biobank certification programme could also add to other national investments in biobanking infrastructure, such as shared or centralised facilities. Biobank certification is predicted to bring benefits to researchers, by increasing the numbers of quality biospecimens available through biobanks (Matzke et al. 2012). Biobank certification is also predicted to benefit individual biobanks, as supplying samples of sufficient quantity and quality allows biobanks to receive contributions such as manuscript co-authorship, and cost reimbursement (Riegman et al. 2015). Our own research has identified significant gaps and variability in the practices of NSW cancer biobanks, which were more pronounced in smaller, restricted-access biobanks, which in turn represented approximately half of our cancer biobank cohort (Rush et al., 2015, Rush and Byrne, 2016).

In view of what has been described as a crisis of research reproducibility (Baker, 2016), Australia needs to radically improve its support and oversight of biobanking, so that Australian research has the best possible chance of successful research translation, both locally and internationally. Irreproducible pre-clinical data are believed to be largely responsible for the failure to translate research results to the clinic (Buck 2015; Freedman et al. 2015; Ioannidis 2014). While the generation of irreproducible data may achieve short-term gains for researchers in the form of publications and further funding, this can lead to years of wasted effort from potentially numerous research groups who attempt to replicate and/or extend these results, as well as wasted research funds (Ioannidis 2014). Furthermore, where irreproducible results contribute to clinical trials or other patient interventions, these can result in patients being administered treatments that do not work (at best) or produce active harm (at worst). In both these cases, potentially effective treatments can also be wrongly withheld, and health care resources wasted.

Biological reagents and reference materials have been described as the largest single contributor to irreproducibility of pre-clinical results (Freedman et al. 2015). Some 40% of health research employs biospecimens, and most of these biospecimens enter the research pathway through biobanks and pathology facilities. An analysis of the numbers of biospecimens used in different cancer research programmes revealed that the numbers of biospecimens employed increased six-fold between 2001-2003 and 2010-2012, and average cohort sizes increased from ~50 to 200 cases (Braun et al. 2014). This requirement for increased sample numbers is also driven by the need for independent test and validation cohorts, to provide pre-clinical data suitable for further translation (Rush et al., 2015). The increasing demand for biospecimens in research strongly argues for a greater need for oversight of the biobanking sector.

In the face of these growing challenges, Australia's biobanking sector remains fragmented, poorly regulated and incompletely defined, and lags well behind that of many countries. In countries such as Canada, Spain and France, national support has allowed biobanks to be identified, networked, evaluated, and supported (Watson et al. 2010, Morente et al. 2011, Rial-Sebbag and Pigeon, 2015). This is of vital importance for biobanks to conduct their activities in accordance with internationally-accepted best practices, and thereby most effectively support research. Biobank networking would be invaluable in an Australian context, as our geographic reality of a small population spread over a large area has led to hundreds of individual biobanks, the exact number of which is presently unknown. In the absence of a national approach to biobanking, there is no way to identify all biobanks, and we consequently have no national biobank register. As such, biobank networking, with its many advantages (to be further outlined in this submission), is poorly developed in Australia.

Furthermore, in the absence of any top-down hierarchical structure that mandates biobank activity, there is no agreed national biobanking standard that biobanks are advised to work towards and maintain. Use of biospecimens in research is currently regulated through individual human research ethics committee (HREC) approval, which largely focusses on processes for donor consent, and the storage and use of associated data to preserve donor privacy. HREC approval of biobanks makes no or few explicit demands regarding the quality of stored biospecimens, and whether these biospecimens are fit for their intended research purpose(s). In summary, our current lack of biobank oversight means that we currently do not know how many biobanks exist in Australia, how most of these biobanks operate, and whether they are effectively supporting Australian research by performing at internationally-accepted standards.

Question 1: Are there other capability areas that should be considered?

Question 2: Are these governance characteristics appropriate and are there other factors that should be considered for optimal governance for national research infrastructure.

Question 3: Should national research infrastructure investment assist with access to international facilities?

National infrastructure investment should allow Australian research to perform at a standard that is comparable to that internationally. As an indirect consequence, this allows Australian research infrastructure to engage effectively with international efforts that are operating according to world's best practice.

Question 4: What are the conditions or scenarios where access to international facilities should be prioritised over developing national facilities?

Question 5: Should research workforce skills be considered a research infrastructure issue?

We agree that research infrastructure support should permit research workforce training, particularly when this training enables infrastructure-associated staff to obtain knowledge and maintain activities that permit a broad sector of Australian research to align with international best practices, and to produce robust and reproducible results that will be suitable for further translation.

The example provided by this submission concerns biobank certification, which is being introduced in a voluntary capacity within NSW by NSW Health Pathology, with additional financial support in 2016 from Cancer Institute NSW. NSW Health Pathology launched their certification programme in June 2016, which has involved customising an existing, highly successful Canadian biobank certification scheme for use in NSW biobanks and pathology laboratories. This biobank certification programme was established by the Canadian biobank network CTRNet, in response to strong support from Canadian biobank stakeholders (Matzke et al. 2012). The CTRNet certification programme is built around a series of education modules which cover every aspect of biobanking, and offers recommended operating procedures and associated standard operating procedures which can be customised for individual biobank use. From our own research conducted in NSW cancer biobanks, there was widespread interest in obtaining standardised standard operating procedure (SOP) templates, particularly from restricted-access cancer biobanks (Rush and Byrne, 2016). Workforce education is therefore the major focus of the biobank certification programme in NSW. By registering for certification, biobanks can also be captured within an on-line registry, which

is a fundamental requirement for subsequent biobank networking and rationalisation of further investment.

The CTRNet certification programme was developed through national support at a cost of \$1,300,000 over 3 years. Some 110 Canadian biobanks have so far registered with the programme, with close to 500 individuals receiving the associated education programme. The adoption of the CTRNet certification programme in NSW therefore capitalises on these previous international investments. NSW Health Pathology have invested additional funds and resources in order to adapt the education modules for use within Australian health and medical research sector, and to develop a new module, specifically for the education of staff employed in pathology laboratories. NSW Health Pathology has also developed a testing programme for each education module that involves reaching a pass mark. In collaboration with CTRNet, NSW Health Pathology has developed an online interface through which education modules can be accessed, and through which the overall certification process is managed. Education modules can also be accessed by researchers, HREC and research governance staff, and other stakeholders seeking to improve their understanding of biobanking.

Since launching the NSW Health Pathology certification programme in June 2016, a number of local consultation meetings have been conducted where a total of 78 researchers and biobankers have attended, providing survey responses from up to 72 individuals. So far, 17 biobanks have registered for certification, with an additional 34 meeting attendees intending to register their biobank for certification. The response to the launch of biobank certification in NSW has thus been overwhelmingly positive.

Question 6: How can national research infrastructure assist in training and skills development?

As summarised in our response above, biobank certification represents a low-cost, scalable solution to training biobank staff that could be extended across the national biobanking sector with national support. We have already received enquiries from NSW biobanks about the possibility of a national certification scheme. As will be outlined further in our response to Q. 15, some Australian biobanks are already forming national networks, and the availability of certification for NSW members of biobank networks but not others will become increasingly problematic as the benefits of certification are realised. Registration for biobank certification also captures biobank identities, and could form the basis of a national biobank register which could be built upon further to establish more comprehensive and effective biobank networks.

Question 7: What responsibility should research institutions have in supporting the development of infrastructure ready researchers and technical specialists?

Question 8: What principles should be applied for access to national research infrastructure, and are there situations when these should not apply?

Question 9: What should the criteria and funding arrangements for defunding or decommissioning look like?

Question 10: What financing models should the Government consider to support investment in national research infrastructure?

Question 11: When should capabilities be expected to address standard and accreditation requirements?

Capabilities should be expected to address standard and accreditation requirements when these requirements pertain to a majority of researchers contributing to a broad field where results aim to influence downstream practices such as clinical care. An example is the use of biospecimens for pre-clinical research which is conducted with the eventual aim of informing clinical practice. The increasing demand for biospecimens in research strongly argues for a greater need for oversight within this sector (Rush et al., 2015). It has been argued that achieving the strict standards required for genome based medicine will require a level of biobank oversight achievable through either voluntary accreditation/ certification, or an official regulatory framework (Browman 2012). Stand-alone biobanks have been reported to experience increased difficulty in quality management and standardisation implementation, with challenges relating to a lack of harmonised SOPs and biobanking guidelines (Zhang et al. 2015). These findings were supported by our own published analyses of cancer biobanks in NSW (Rush et al., 2015, Rush and Byrne, 2016), and are very likely to apply elsewhere in Australia.

Question 12: Are there international or global models that represent best practice for national research infrastructure that could be considered?

Australia's biobanking sector might be expected to be similar to that of Canada, as Australian and Canadian peak medical research funding bodies have comparable annual budgets, and similar goals (Rush et al., 2015). National funding via the Canadian Institute of Health and Research has led to a well-established and successful nation-wide biobank network, where individual biobanks are funded by host institutions, non-profit organizations, grants, and cost recovery. Funding for the Canadian Tumour Repository Network (CTRNet) is restricted to the provision of network activities, such as certification programmes, SOP's and biobanking policies (Watson et al. 2014). We argue that a similar level of national funding in Australia would permit national extension of the NSW Health Pathology biobank certification scheme launched in 2016.

Question 13: In considering whole of life investment including decommissioning or defunding for national research infrastructure are there examples domestic or international that should be examined?

Question 14: Are there alternative financing options, including international models that the Government could consider to support investment in national research infrastructure?

Health and Medical Sciences

Question 15: Are the identified emerging directions and research infrastructure capabilities for Health and Medical Sciences right? Are there any missing or additional needed?

We strongly endorse the focus upon virtual collaborative biobank networks.

Biobank networks allow the establishment of streamlined, harmonized or shared biospecimen application processes, to provide researchers with easier access to larger sample cohorts, while at the same time increasing the use of stored biospecimens. This reduces unnecessary duplication of

effort, increases the uptake and use of best practices, and ensures that local biobank resources are used with maximal efficiency. Biobank networking can also lead to increased visibility of individual biobanks, and of biobanking more broadly, potentially leading to much-needed further investment in biobanking. The combined benefits of biobank networking lead to improved researcher access to quality biospecimens, which is an important driver of both national and international research collaborations. Access to quality biospecimens is also required for the implementation of new technologies such as massively parallel sequencing into the clinic, and for industry use of stored biospecimens. These benefits will in turn produce better quality, more reproducible research results that are more likely to be successfully translated for the benefit of patients, carers and the supporting health system.

Given the obvious advantages of biobank networking, Australian biobanks are beginning to self-organise into local and national networks. Within NSW, the Cancer Institute NSW supported Biospecimens Stakeholders Network has supported numerous collaborative research projects to improve cancer biobanking (Rush et al., 2015, Rush and Byrne, 2016). Two paediatric cancer biobanks in Sydney have recently networked under a common governance framework to form the Sydney Children's Tumour Bank Network, and are developing a shared biobank database with philanthropic support from The Kids' Cancer Project.

At a national level, Brain Cancer Biobanking Australia (BCBA, <http://www.bcba.org.au/>) was recently established under the umbrella of the Cooperative Trials Group for Neuro-Oncology (COGNO) with the goal of accelerating brain cancer research and the translation of that research into improved outcomes in patient care. BCBA is committed to supporting research performed by clinicians and scientists working in both the paediatric and adult brain cancer fields. In 2016, BCBA established an internet-based biospecimen register, and is currently finalising a common biobank access form, to reduce the administrative burden upon researchers who need to apply to multiple brain cancer biobanks. BCBA has leveraged support from a number of sources (Cancer Council NSW, Roche, DDB Remedy and philanthropic groups dedicated to brain cancer, namely the Isabella and Marcus Paediatric Brainstem Tumour Fund, Mark Hughes Foundation, and Robert Connor Dawes Foundation). BCBA is operating entirely without government support. Paediatric and adolescent/young adult (AYA) biobanks have been recently awarded philanthropic funding by The Kids' Cancer Project to form a network across Australia and New Zealand. This network will include all 9 existing paediatric/AYA biobanks in Australia and New Zealand, and will operate as an official sub-committee of the Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG). Shared committee representation across local and national cancer biobank networks ensures that they operate in a harmonised fashion, and will not duplicate activities. For example, solutions to problems such as the need for network-wide sample application forms can be passed between networks to accelerate the pace of change with minimal resourcing. However, the work of these biobank networks is being rendered more difficult in the absence of a national approach to biobanking, with associated national support. Biobank networks across state boundaries would greatly benefit from a single framework against which all activities would be bench-marked. For example, NSW biobanks currently are able to register for certification, but biobanks from other states within the same network cannot.

The cancer biobank networking described above is being supported by NSW government funding, industry and philanthropy, with the latter also being a major supporter of the biobank sector

elsewhere in Australia. Philanthropy has provided outstanding support to biobanks, and is continuing to do so in the absence of national biobanking support. The lack of national biobank support risks sending the message to philanthropy and industry that their support is not recognised or valued, and that biobanking itself is of little significance.

Question 16: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

Australia's biobanking sector falls well short of that in other countries. Other countries such as Canada, France, and Spain have invested in national biobanking programmes which allow for the development of networks. Biobanks across Europe are also benefiting from major infrastructure initiatives such as BBMRI-ERIC. 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.

Question 17: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Health and Medical Sciences capability area?

Environment and Natural Resource Management

Question 18: Are the identified emerging directions and research infrastructure capabilities for Environment and Natural Resource Management right? Are there any missing or additional needed?

Question 19: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

Question 20: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Environment and Natural Resource Management capability area?

Advanced Physics, Chemistry, Mathematics and Materials

Question 21: Are the identified emerging directions and research infrastructure capabilities for Advanced Physics, Chemistry, Mathematics and Materials right? Are there any missing or additional needed?

Question 22: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

Question 23: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Advanced Physics, Chemistry, Mathematics and Materials capability area?

Understanding Cultures and Communities

Question 24: Are the identified emerging directions and research infrastructure capabilities for Understanding Cultures and Communities right? Are there any missing or additional needed?

Question 25: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

Question 26: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Understanding Cultures and Communities capability area?

National Security

Question 27: Are the identified emerging directions and research infrastructure capabilities for National Security right? Are there any missing or additional needed?

Question 28: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

Question 29: Is there anything else that needs to be included or considered in the 2016 Roadmap for the National Security capability area?

Underpinning Research Infrastructure

Question 30: Are the identified emerging directions and research infrastructure capabilities for Underpinning Research Infrastructure right? Are there any missing or additional needed?

Question 31: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

Question 32: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Underpinning Research Infrastructure capability area?

Data for Research and Discoverability

Question 33: Are the identified emerging directions and research infrastructure capabilities for Data for Research and Discoverability right? Are there any missing or additional needed?

Question 34: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

Question 35: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Data for Research and Discoverability capability area?

Other comments

If you believe that there are issues not addressed in this Issues Paper or the associated questions, please provide your comments under this heading noting the overall 20 page limit of submissions.

References cited in this submission

Baker, M 2016 '1500 Scientists Life the Lid on Reproducibility', *Nature*, vol. 533, no. 7604, pp452-454.

Braun, L et al. 2014 'Individual investigator profiles of biospecimen use in cancer research', *Biopreserv Biobank*, vol. 12, no.3, 192 – 198.

Browman, GP 2012 'Special series on comparative effectiveness research: challenges to real-world solutions to quality improvement in personalized medicine', *J Clin Oncol*, vol. 30, no.34, 4188 – 4191.

Buck, S 2015 'Solving reproducibility', *Science*, vol. 348, no. 6242, pp. 1403.

Freedman, LP, Cockburn, IM, Simcoe, TS 2015 'The Economics of Reproducibility in Preclinical Research', *PLOS Biology*, vol. 13, no.6.

Ioannidis, JPA et al. 2014 'Increasing value and reducing waste in research design, conduct, and analysis', *The Lancet*, vol. 383, no. 9912, pp. 166 – 175.

Matzke, EAM 'Certification for biobanks: the program developed by the Canadian Tumour Repository Network (CTRNet)', *Biopreserv Biobank*, vol. 10, no. 5, pp. 426 – 432.

Morente, MM et al. 2011 'Managing a Biobank Network', *Biopreserv Biobank*, vol. 9, no.2, pp. 187 – 190.

Rial-Sebbag E 'Regulation of Biobanks in France', *J Law Med Ethics*, vol. 43, no. 4, pp. 754 – 765.

Riegman, P et al. 2015 'Optimizing sharing of hospital biobank samples', *Sci Transl Med*, vol. 7, no. 297, pp. 297.

Rush, A et al. 2015 'Biobank classification in an Australian setting', *Biopreserv Biobank*, vol. 13, no.3, pp. 212 – 218.

Rush A and Byrne JA 2016 'Optimizing sharing of hospital biobank samples', *Clin Biochem*, vol. 49, no. 7, pp. 492 – 497.

Watson, PH et al. 2010 'Canadian Tumor Repository Network. Biobank Profiles', *Biopreserv Biobank*, vol. 8, no. 4, pp. 181 – 185.

Watson PH et al. 2014 'A framework for biobank sustainability', *Biopreserv Biobank*, vol. 12, no. 1, pp. 60 – 68.

Zhang L et al. 2015 'Establishment of a network-based intra-hospital virtual cancer biobank', *Biopreserv Biobank*, vol. 13, no. 1, pp. 43–48.

Signatories to this submission

- NSW Health Pathology (Professor Roger Wilson, Chief Pathologist; Ms Jane Carpenter, Program Manager, Biobanking Services)
- Australian and New Zealand Children's Haematology/Oncology Group (Dr Chris Fraser, Chair)
- Brain Cancer Biobanking Australia (Professor Anna Nowak, Co-Chair; Professor Michael Besser, Co-Chair; Ms Robyn Leonard, Founder; Dr Mythily Mariasegaram, Project Officer)
- Sydney Children's Tumour Bank Network (Ms Amanda Rush, Chair)
- Children's Hospital at Westmead Tumour Bank, NSW (A/Prof Daniel Catchpoole)
- Monash Children's Cancer BioBank, VIC (Dr Peter Downie)

- Telethon Kids Institute, WA (Dr Nick Gottardo)
- Women and Children's Hospital, SA (Dr Maria Kirby)
- Children's Cancer Centre Tissue Bank, Royal Children's Hospital, Murdoch Children's Research Institute, VIC (Prof Richard Saffery, Dr Françoise Mechinaud, Dr Louise Ludlow)
- Children's Cancer Institute Tumour Bank, NSW (Dr Jamie Fletcher)
- Queensland Children's Tumour Bank (University of Queensland) and the Lady Cilento Children's Hospital, Qld (Dr Andrew Moore)
- Cancer Society Tissue Bank, Christchurch NZ (Dr Siobhan Cross)