Submission
2016 National Research Infrastructure Roadmap Capability Issues Paper

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Background and Summary

The Australian Genome Research Facility is Australia's major National Research Facility supporting and collaborating with Australia's genomic science and industry sectors. AGRF is a not for profit organisation established to ensure researchers have full access to the required and leading edge genomics platforms within Australia. AGRF:

- is Australia's largest genomics service provider and collaborator;
- is headquartered in Melbourne (moving to the new Victorian Comprehensive Cancer Centre (VCCC) in 2017) with major hubs in Sydney, Brisbane, Adelaide and Perth;
- has Australia's most comprehensive range of genomics platforms and bioinformatics, services, collaborators and clients;
- has strong relationships with all relevant key institutions and commercial sectors;
- is the only NCRIS-funded capability offering the full range of genomic platforms and services.

  AGRF has more than 3000 clients and research collaborators in the biomedical (66%), environmental (9%) and agriculture (24%) sectors, from universities (58%), research institutions (26%), industry (5%), government (4%), hospitals (3%) and others (4%).

AGRF is contributing to the Australia's national policies, capacity building and ongoing competitiveness by providing national leadership in new initiatives such as the recently announced Genome Innovation Hub (which will acquire, test, develop and apply cutting edge genomics technologies to address high priority research needs), and the Genome Australia proposal currently being developed with the genomic research community.

Before addressing the Issues Paper's direct questions, it is critical to comment on the position and future significance genomics holds for Australia's science, the economy and international competitiveness. The "Omics" (genomics, proteomics, metabolomics, phenomics and a number of "subsets" of these, together with bioinformatics) are "next generation" sciences requiring government investment. While all "omics" warrant support, this should be in proportion to the comparative assessed benefit from each of them. Assessment of the research outputs and potential applications of the "omics" clearly indicates that genomics is well ahead of the others. Genomics has evolved from an understanding and application of a new science to a truly disruptive technology critical to Australia's research and business development futures. Genomics is now a critical enabling technology in all areas of the life sciences.

Australia's genomic needs are best met through a coordinated national capability, such as AGRF and the emerging "Genome Australia model" (GA), networking with the key institutions and researchers.

Genomic technologies are now more mainstream (i.e. critical for research and business). User institutions

now have easier and more cost-effective access to the technologies. The rapid expansion of sequencing outcomes with consequential reductions in unit cost are well known. However, it would be naïve and inefficient to base Australia's genomics needs from a dispersed model based on individual centres/laboratories purchasing their own platforms. Experience has demonstrated that, despite the increasing accessibility of the platforms the national approach needs to address the following:

1. The capabilities in the researcher community in relation to genomics range from "mature" to "naïve". Many potential users require advice on the benefits and resourcing required (see question #2 response);
2. The range of genomics platforms, (Sanger, Next Generation, Microarray, DNA Methylation, genotyping, bioinformatics systems to name a few) and the expertise to operate them is beyond the scope of even some of our largest research institutions. To meet the full spectrum of national needs, these facilities require supporting capabilities (project design, bioinformatics, library creation and curation, DNA extraction and commercial genomics advice to industry and the qualified and accredited personnel and systems to run them to name a few);
3. There are significant real costs in maintaining this capability (maintenance contracts, consumables, qualified technicians, LIMS and bioinformatics services);
4. There are risks to data quality and potential loss of intellectual property from using international service providers. AGRF's experience has seen a significant number of Australian collaborators/clients who switched to international providers (usually based on cost) becoming disillusioned with the output they have received, for the reasons listed, and returning to AGRF.
5. The need for scale and coordination to adequately address the nation's priorities and allow engagement at the international level. Although sequencing to an extent has become democratised on a small scale, researchers or nations will always push the boundaries of the technology to address large scale problems (eg 100K, 1M genomes projects, etc). Furthermore, Australia must develop and maintain such capacity in order to be a player and engage in such important international initiatives.

Policy makers need to appreciate and accommodate the diversity and complexity of the genomics sector if we are to adequately to address the national need.

Internationally there is a tremendous race between nations to capture the global intellectual capacity in genomics (see question #4 response), Australia's competitiveness and future opportunities in the medical, agricultural and environmental sectors requires recognition and support for a national coordinated genomics capability.

Whist individual institutions and universities may seek to purchase genomics equipment, Australia's national needs require scale and diversity. Genomics is transforming agriculture and medicine, providing powerful new research tools and delivering significant opportunities for agriculture and improvements in human health. The newly emerging science of environmental genomics offers new opportunities for this sector Genomics is not just another "omic". It is of greater importance and significance to researchers than the other "omics" combined. This importance is expected to increase

for the reasons outlined in this response, warranting classification in Section 10 "Underpinning Research

Infrastructure".

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

AGRF has consulted with a cross section of its research collaborators and industry clients on this question. Whilst strongly endorsing the intent of the Roadmap/Issues Paper the general consensus is:

1. There is a perceived imbalance in the recognition of critical areas of opportunity reflected in the Capability Focus Areas. These include Agriculture (including Food) and Systems Biology. These nominations reflect the need to consider "capability areas" based on both sector and key disciplines.
2. There is also disappointment with the treatment of genomics given its acknowledged enabling role in all aspects of science and industry, in critical areas such as the emergent revolution in clinical genomics based on the community and personal health application of whole genome sequencing.

Our submission's general introduction outlines the rationale for this consensus. Genomics has now developed as a cost effective technology and platform essential to the advancement of all fields, sectors and human endeavours. It is essential the NRI capability be capable of addressing this diversity of need and opportunity. It is important to reiterate genomics is now a critical enabling technology in all areas of the life sciences.

The consultation process is an opportunity to correct the current Roadmap imbalances as well as the opportunity develop a more harmonised, coordinated and effective national capability and performance built on Australia's current dispersed research, practitioner and funding landscape (institutional, departmental, NHMRC, ARC etc). Harmonisation includes strategic consideration of more coordination and targeted investment between by the funding bodies to assist in the development of a greater national capacity. It also provides the opportunity for inclusion of social and economic considerations in the development and application of genomics base sector solutions and products.

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

Bioplatforms Australia (BPA) currently has the overarching coordinating and prioritising of funding roles relevant to the "omics" in general under NCRIS. AGRF benefits from a continuing close partnering and operating relationship with BPA, most recently reflected in the successful collaboration between BPA, AGRF, Ramaciotti and University of Melbourne through the NCRIS Agility Fund.

Australia's genome services and capabilities are currently located in a small number of specialist scaled and comprehensive facilities (e.g. AGRF, Ramaciotti) and scattered research laboratories in major institutions with a specific dedicated focus (e.g. WEHI, Ramaciotti and QIMB). There are also a few individual platforms and bioinformatics capabilities in various institutional departments and laboratories. This has arisen for a number of legitimate reasons including in the first instance the need for a scaled and contemporary capability to effectively compete against and/or collaborate with major international research groups. Governance of national research infrastructure also needs to address the issues of data quality and threats to the protection of intellectual property (see International issues in questions #3 # 4 responses).

These arrangements have evolved to meet both the opportunity to embrace genomic capabilities as well as recognising the contribution of the technology. In more recent times a wide cross section of the

genomics community has been exploring how the current arrangement can be further developed – Genome Australia (GA). This has involved input/support from >130 active researchers and related practitioners, major institutions, AGRF and BPA. As a broad underpinning technology with scope for large scale engagement across several areas of the life sciences at national and international level, genomics should have an appropriate governance structure. Whilst the GA concept is still being developed, it is suggested the Taskforce should consider it as part of its deliberations.

The GA "National Purpose" has been defined as a more coordinated and inclusive network for the "exploitation of genomic opportunities for the benefit of the Australian economy and the country's global standing". This would also provide the pathway for increased integration of genomics in infrastructure, funding and interoperability with other NCRIS capabilities and international programs and collaborations.

AGRF supports this consideration as it would complement and support the current genomics diversity of landscape whilst strengthening the national coordinated capability and international competitiveness and collaboration attractiveness. An opportunity to build on the current capabilities through enhanced coordination of effort and subsequent efficiencies in scale, harmonization in approach, standardization of methods, minimization of duplication and the environment in which collaboration within and between initiatives and sectors is encouraged.

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

The immediate answer to this question is "yes". Australia's capacity and performance in genomics is dependent on forging and maintaining key international linkages at the policy, funding and operational levels.

Australia whilst an important contributor to global science and innovation, remains a small economy compared to its peer science nations. Equally important, there is a global "discovery race" between the major genomics nations, driven by the objective of better delivery of solutions for the range of challenges and opportunities as well as the competitive tension of capturing the knowledge and intellectual capacity in genomics.

Global programs critical to Australia's interests through collaboration/partnering are numerous, well documented and include: Genome Canada, Global Alliance for Genomics and Health and Obama Precision Medicine Initiative, US Cancer Moonshot, US NIH Centres for Common Disease Genomics, NIH Population Scale Sequencing, Genome England, European Molecular Biology Laboratory (EMBL), UK NHS 100,000 Genomes Project and Translational Medicine initiatives, Earth Biome Project and ELIXIR. Similar initiatives of direct interest to Australia are occurring in numerous other countries including France and Singapore. Programs of this nature and scale tackle problems of global significance requiring global engagement. Engaging and leading international programs gives Australia early access to key genomic information, capacity building and industry engagement. It also provides the opportunity for Australian researchers, clinicians and industry to benefit from high impact globally programs.

Such global initiatives are substantially resourced, resulting in collective expenditures of many billions of dollars, for example the Obama Precision Medicine Initiative provides a $215 million NIH investment that

includes:

- $130 million to NIH for development of a voluntary national research cohort of a million or more volunteers to propel understanding of health and disease and set the foundation for a new way of doing research through engaged participants and open, responsible data sharing;
- $70 million to the National Cancer Institute, part of NIH, to scale up efforts to identify genomic drivers in cancer and apply that knowledge in the development of more effective approaches to cancer treatment;
- $10 million to the Food and Drug Administration to acquire additional expertise and advance the development of high quality, curated databases to support the regulatory structure needed to advance innovation in precision medicine and protect public health;
- $5 million to the Office of the National Coordinator for Health Information Technology to support the development of interoperability standards and requirements that address privacy and enable secure exchange of data across systems.

In the UK, the 100,000 Genome Project committed $375 million for the introduction of clinical genomics (whole genome sequencing diagnostics) into the National Health Service (NHS). France is committing $745 million to develop clinical genomics capability as a key component of routine healthcare.

Collaborations and partnerships with programs such as these provides access to programs not usually automatically available or of a scale Australia can support independently.

In response, Australia needs to have the coordinated budget, operational and intellectual scale to credibly collaborate. As well as a traditional emphasis mutual research interest/institution approach, the Roadmap needs to accommodate the wider issue of “knowledge” capture and access from such interactions. Australia needs to develop its own infrastructure and capability in order to collaborate on an equal footing.

Most of the global initiatives are seeking to create a network of sequencing, genotyping, interpreting and translational capabilities. It is critical that Australia partner in international endeavors, both as a contributor of unique data and beneficiaries of the global body of work that comes from being an active participant.

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

International linkages should provide access to high end infrastructure that is not fiscally feasible or sensible to replicate in Australia. However, relationship credibility requires investment in national facilities. These also result in the development of local capability, skills, and knowledge prioritised to Australian research needs, rather than what international facilities might wish to focus on. Critical international linkages provide Australia with a “seat at the table” for significant international initiatives and collaborations.

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

Trained and skilled personnel (Intellectual Capital) are essential "infrastructure" of any designated capability. Lack of this is recognised as a significant impediment to the uptake and effectiveness of some current genomic investment, particularly in the smaller laboratories that lack scale and resourcing.

Similarly, the provision of the capability to deliver this training and infrastructure needs to be addressed in the context of this question. AGRF currently undertakes this role through its nodes and networks. However, this contribution to the national genomics agenda is limited by lack of funding at a scale required to meet national requirements.

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

Further to the response to question 5, NCRIS-funded experts should be available to provide specialist training and support activities. AGRF's current training and skills development program provided regionally through its nodes and extensive research and industry client/collaborator relations are well suited to be a pathway for this training, if appropriately resourced.

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

The "harmonisation" objective referred to above would be greatly assisted if the research institutions and traditional funding entities, (eg ARC, NHMRC, R&D Corporations and CRCs) were encouraged to:

1. Direct researchers seeking funding for genomic services or platform purchase to the designated NCRIS facility for the provision of these services unless a dedicated facility is justified. This would address much of the current inefficiency in utilisation of expensive platforms that:
    - 1) have a high rate of obsolescence due to rapid development of the technologies/platforms (unlike Microsoft, the current dominant supplier of genomics platforms does not usually provide Interoperability" between upgrades and/or new platforms); and
    - 2) have high maintenance contract and consumables costs. Ffacilities of the scale and diversity such as AGRF have the ability to minimise these due to it market size to attracting substantive discounts on purchases and consumables.
2. Favour the use of local facilities that provide formalised training and support activities, rather than overseas options that do not provide the necessary level of interaction and coaching to support their research needs.

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

There are a range of "Principles" that should be applied. Those of national relevance and potential benefit against national targets, along with merit and excellence/track record should be supported.

National infrastructure support and investment needs to address accessibility. This needs to take into consideration a number of aspects:

1. All current and potential users needing the technologies and associated facilities for their research or business need to be accommodated;
2. This need to consider the needs of the experienced and new users, the specific testing requirements of the user (in genomics, technologies, platforms protocols and subsequent bioinformatic, data QA and interpretation treatments are dictated by the user needs); and
3. The access and costing policies applied and considered in infrastructure policy development should be transparent and comparable, often institutions are not aware the true cost of undertaking an activity in house, frequently referring to the direct costs only. Without this awareness, funding agencies may not be aware of the true cost of providing a facility.

Researchers, institutions and providers of genomics need to comply with designated procedural, accreditation, quality assurance and knowledge/data security standards, consistent with the research quality management system (rQMS) mentioned in the Issues paper.

It is worthwhile referencing key elements of criteria applicable the early days of NCRIS:

1. Australia's investment in research infrastructure should be planned and developed with the aim of maximising the contributions of the R&D system to economic development, national security, social wellbeing and environmental sustainability;
2. Infrastructure resources should be focussed in areas where Australia is, or has the potential to be, world-class (in both discovery and application driven research) and provide international leadership;
3. Major infrastructure should be developed on a collaborative, national, non-exclusive basis. Infrastructure funded through NCRIS should serve the research and innovation system broadly, not just the host/funded institutions. Funding and eligibility rules should encourage collaboration and co-investment. It should not be the function of NCRIS to support institutional level (or even small-scale collaborative) infrastructure;
4. Access is a critical issue in the drive to optimise Australia's research infrastructure. In terms of NCRIS funding there should be as few barriers as possible to accessing major infrastructure for those undertaking meritorious research;
5. Due regard be given to the whole-of-life costs of major infrastructure, with funding available for operational costs where appropriate; and

6. The Strategy should seek to enable the fuller participation of Australian researchers in the international research system.[1]

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

(See question #9)

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

As indicated above, facilities should be expected to have made significant progress with NATA-type accreditation within one year of being in receipt of NCRIS support. This is preferable to ensure quality as well as international "comfort" when pursuing opportunities considered in questions 3 and 4. Failure to receive appropriate accreditation, where available, should be a criterion for defunding after a defined grace period (say, 24 months from receipt of funding).

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?

Genomics is a key underpinning, disruptive and enabling technology of this time. As indicated in the Key Summary above, genomics has and continues to develop as one of the most powerful contributors to every aspect of research, industry and living systems in general. This is best seen in the Health and Medical Sciences sector, with the next innovative wave and economy generated being clinical genomics. This will drive the emphasis of community and personal health and wellbeing towards preventative rather than reactive solutions with complementary widespread reductions in costs to this sector and the community in general. The development of this and other revolutions in genomics requires an ongoing adaptive capability that is coordinated, integrated throughout the areas of relevant interest and scale as well as being internationally relevant and connected.

The history and rationale for this approach, particularly in the health and medical sciences was addressed in question #3.

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?

As previously commented the general consensus is that the Roadmap needs to give more extensive and in-depth consideration of this sector, including greater recognition of the differentiation of Agriculture, Food, and Systems Biology.

[1] Personal communication from Mike Sargent

In addition the Roadmap/Issues Paper needs to recognise the wider global challenges and goals relevant to the environment and NRM fields that NCRIS and genomics can contribute solutions to: poverty and hunger, good health and well being, clean water and sanitation. climate change and adaptation to urban and non-urban systems and habitats.

AGRF has contributed to an initiative to capture the views of key national leaders in this field. The key points identified relevant to this question have been:

1. Genomics critical to improving agricultural productivity, sustainability and biosecurity of food production and consumer chain systems, reduce inputs and waste whilst maximising outputs, the introduction of beneficial transformational technologies and systems as well as adapting to long term changes in the environment and food production systems;
2. NCRIS should recognise the opportunities for genomics in the environment, agriculture and NRM fields includes understanding better the plant-soil biome interactions and feedbacks leading to better management of soil health, improved water use efficiency, sustainable development of new production areas and improved resilience to climate events and impacts;
3. Common platforms are required for data handling, IP management, training, barcode curation and links to sensors and phenomics.

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

Supporting the advice in the previous question # 18, AGRF has already contributed to the Earth Microbiome Project via the BPA "BASE" dataset, which was a major landmark in base-lining the microbial composition of Australia's massively diverse soils. An extension of BASE to provide detail on key production characteristics of agricultural soils in particular, for example, disease suppressive soils, would be of substantial future benefit.

Understanding Cultures and Communities

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

A unique proposal identified to AGRF from the Centre for Ancient DNA of the University of Adelaide (reflecting genomic demand outside the traditional arena of Health, Medicine, Environment and Agriculture) is Identification and Repatriation of war dead via the Australian Historical DNA Database . The opportunity for generation of familial genomic databases to allow the identification and repatriation of the remains of war dead diminishes over time. While Australian remains continue to be recovered from the wars of the 20th century, and technologies for the recovery of identifiable genomic information from these improve, the window of opportunity to create meaningful databases of genomic data from their surviving relatives for matching purposes is closing. No existing Australian DNA databases are suitable for this purpose because of significant post-war migration to Australia. The project seeks donations of DNA from anyone (1) born in Australia before 1945 or directly descended from people who were born and living in Australia before 1945.]

National Security

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

The unpredictable nature of biosecurity risk underscores the need for accredited and distributed genomic facilities of suitable scale to meet both surveillance requirements and national emergencies. These facilities should be primed for familiarity with, and responsiveness to, biosecurity research and investigative requirements, possibly through the construction of NCRIS-supported baseline database formation (eg, "Microbiota of Australian Intensive Animal Husbandry Systems") AGRF has the scale and opportunity to better complement this work, particularly that of the AAHL.

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

Following the Human Microbiome Project, international efforts to study wild animal microbiomes (as a source of zoonosis, as well as aspects of conservation biology), farmed animal microbiomes (as sources of baseline "normal" microbiomes and antibiotic resistance incubators), as well as human gut microbiomes at the population level will intensify. Involvement in such programs will greatly assist both national and international coordination in disease outbreak prediction and control.

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?

AGRF has identified a number of operational matters that warrant consideration under this question:

1. The coordination of storage, compilation and data transfer (networks);
2. The establishment of key databases (e.g. clinical exome data, across the country, e.g. might overlap with Australian Genomics Health Alliance) and clarity of who is going to maintain these for the future (ensure permanence) (e.g. see http://exac.broadinstitute.org/)
3. Portals to access all these data;
4. National infrastructure to support projects of national importance, e.g. the National Centre for Indigenous Genomics. National funding is needed to maintain, support and make these data available.

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

Addressed in question 3.

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

AGRF has initiated the creation of a number of Genomics Innovation Hubs (GIH) to access novel data-generating technologies/platforms. This has been extremely well received by the major research institutions and state government policymakers due to the early adoption and globally competitive outcomes, through the earlier availability of the technologies to the Australian science community. The Roadmap should provide funding for nascent research instrumentation to allow early access to new promising and disruptive data generation and data analysis technologies.

Data for Research and Discoverability

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?

At this time, non-academic organisations are excluded from membership of research data networks. This includes NCRIS-supported non-academic entities such as the AGRF. This restriction limits our operational efficiency and our ability to provide collaborative support. For example, AGRF is not eligible for accounts with the Pawsey Supercomputing Centre or National Computational Infrastructure (NCI), Victorian Life Sciences Computational Initiative (VLSCI), or Research Data Storage Infrastructure (RDSI). The definition of eligibility for membership of these networks needs to be broadened to include all entities in receipt of NCRIS funds. This would greatly enhance the collaborative, cross-disciplinary and cross-institutional objectives being sought through the Roadmap and Issues Paper.