Submission
2016 National Research Infrastructure Roadmap Capability Issues Paper

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Submission Details

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Declaration of Interests

Bioplatforms Australia Ltd is constituted by members with an interest and stake in the Australian biomolecular science sector. Bioplatforms Australia manages an NCRIS investment across the Genomics, Proteomics, Metabolomics and Bioinformatics sectors via subcontracts with Universities, Research Institutes and Private entities.

Response Preparation

Contributions to the submission below were canvassed across the Bioplatforms Australia facility network and user communities both via direct communication and recent national consultation facilitated by Dr Susan Pond. Bioplatforms Australia has extensive experience in all levels of national capability development with over 10 years governance and operational activity.

The breadth and depth of national value requires that 'Omics Capability be included as an Underpinning Research Infrastructure as described in Section 10.

The "Issues Paper" should recognise the national value that an investment in 'omics capability brings to the national innovation system. 'Omics science is critical to Life Sciences, encompassing national priorities such as human health and well-being, agricultural productivity, food security, national biosecurity, environmental science and biodiversity conservation. Furthermore, 'omics capability offers depth to the system – discovery research, scientific validation, product and service development and post-production quality and monitoring. 'Omics is currently supported as the collection of genomics, proteomics, metabolomics and supporting bioinformatics. Approximately 50% of NCRIS 'omics investment supports genomics capability.

In all areas of science, new technologies and sensors are driving unprecedented growth in the quantity, diversity and complexity of data. The similarly unparalleled growth in data science and machine learning methods are enabling fundamentally new approaches to scientific discovery and regulation of interconnected systems.

In the life sciences, breakthroughs in high-throughput technologies are enabling detailed investigation of cellular components and interactions at the molecular level. These include technologies to generate data on the variation and regulation of the genome, transcriptome, epigenome, proteome and metabolome. The application of these molecular approaches is illuminating the intricacies of living matter across widely different scales, from the molecule to the cell to the patient, from the organism to the biosphere.

Correlation of big data sets from fully sequenced genomes to phenotypic information will make personalised medicine possible, optimise growing conditions for crops and animals in our food supply, modify organisms for production of renewable materials and bioactives and enable understanding and conservation of entire natural ecosystems.

These advances will not be achievable without cutting-edge research infrastructure together with bioinformatics expertise to undertake coherent analysis of the massive data sets that are generated.

The following submission outlines the value of 'omics infrastructure to the research sector, from basic to applied, academic to industrial, biomedical to agriculture and environmental sciences. If done well, investment in 'omics capability will yield innovative opportunities of national importance, international scale and in fledgling fields such as synthetic biology.

Life Sciences is an Australian research strength

The Life Sciences sector, incorporating *Biological Sciences*; *Agri-food and Veterinary Sciences*; *Biotechnology* and *Medical and Health sciences* collectively, represent approximately 33% of the national research output with approximately 80% rated at or above world standard (>3; ERA 2015). The Issues Paper identifies closely correlating Capability Focus Areas including

- Health and Medical Science
- Environment and Natural Resources
- Understanding Cultures and Communities
- National security
- Underpinning Research Infrastructure
- Data for Research and Discoverability

The 'omics (and crucial underpinning informatics) is a key enabling capability for Australia's National Science and Innovation Priorities.

‘Omics underpins life sciences

The ‘omics capability extends far beyond discovery science to ongoing monitoring of biological systems – manufacturing of biologicals, clinical trials, food quality and environmental health and rehabilitation are all supported by access to biomolecular capability and as such ‘omics is one of the true enablers of the Australian research and innovation system.

The ‘omics capability includes a continuum of

- Genomics (sequencing of DNA)
- Transcriptomics (sequencing of RNA as an indicator of DNA expression)
- Proteomics (analysis of protein complement as an indicator of DNA and RNA translation)
- Metabolomics (analysis of metabolites as an indicator of protein function)
- Bioinformatics (analysis of the data outputs from all of the above, as discrete capabilities and as integrated informers of “systems biology”)

Genomics is a foundational science, has been and will continue to grow as a critical national capability. It’s value is strategically enhanced through augmentation with analysis of proteins, metabolites and the integration of these datas to ensure a holistic perspective of biology. Genomics investment accounts for approximately 50% of the total current NCRIS investment in ‘omics. The prominence of genomics is articulated through submissions made by the Australian Genome Research Facility (NCRIS supported) and Genome Australia (proposed concept).

The inclusion of phenome (observation and description of whole living systems) is inextricably linked to biomolecular ‘omics capability and has over the past decade been resourced via linked but different capabilities.

Work has begun through NCRIS to enable the potential of Australian science in these domains and continued investment is necessary to deliver national social and economic benefit.

The provision of genomics and ‘omics capability for research, clinical research and clinical operations should be noted. The broad research communities serviced and breadth of research applications should be contrasted to the controlled outputs required at the clinical interface, often used within health systems to inform clinical decision making.

The existing Bioplatforms Australia (BPA) facilities are capacity constrained within the existing funding envelope.

Life Sciences are now a big data Science

Life sciences are now a big data science. For example, in the past 4 years the number of DNA samples alone being analysed by next generation sequencing per annum (at NCRIS BPA) has risen from 1000 to greater than 30,000. Experimental scale, combined with increased throughput has resulted in a data deluge requiring a different set of skills from that of a decade ago. Data analytics, computational science, biostatistics, software engineering and data visualisation are now as important as biochemistry and molecular biology. Extension of molecular analysis to phenotype remains a significant challenge that will ultimately provide insight and value across the breadth of Life sciences. The ‘omics capability requires both embedded bioinformatics and close affiliation with the eResearch communities described in the underpinning and data sections of the issues paper.

International connectivity is necessary

Science and research are not siloed by Australia’s coastline. Engagement internationally allows significant national benefit (often multiplicative) through scaled programmes in human genomics, harmonised methodological adoption in environmental surveying and inclusion in significant agricultural research and development that is only possible that is only possible if Australia is a contributing global scientific citizen. National scale research infrastructure permits Australian scientists to engage in big science collaboratively, join international endeavours with critical mass and share outcomes in a way that is not possible within institutional silos. Additional investment is necessary in international engagement and research infrastructure such as involvement in the Pan-European ELIXR bioinformatics network will enhance our connectivity.

Big science is happening

National Capacity is required for Australia to meet existing and new obligations in science of scale and complexity.

The ASPREE study (Monash), 45 and Up Study (Sax Institute), Genomics Health Alliances (NHMRC, Victoria, NSW, ACT), Environomics Future Science Platform (CSIRO), Centres of Excellence, NHMRC Programme Grants and CRCs all require capacity, capability and collaborative contributions from ‘omics research infrastructures that are by design accessible and at scale.

The critical genome sequencing infrastructure and sophisticated pipelines required by the programmes are and will be accessed through BPA facilities.

The opportunity to build exciting big science occurs as a consequence of national research infrastructure – the Melanoma Genome Project, BASE (continental soil survey), Great Barrier Reef project, OzMammals genome initiative, Stem Cells consortia and investigation of antibiotic resistance are but some of the initiatives that only occurred as a consequence of national scale investment in ‘omics, and all address national challenges of significance at scale in collaborative environments.

Industry engagement is critical

‘Omics capability, inclusive of dedicated bioinformatics expertise, supports the continuum of the innovation system from discovery research through product development, clinical and field trials, product QC, new health, environmental and conservation services. Strategic support for applied programmes, be they direct end user engagement or through organisations such as CSIRO, the Rural Development Corporations, CRCs and government organisations is crucial. Industry investment builds on and multiplies government investment, but are insufficient in isolation from the broader system to deliver the capacity required for systemic value.

Specific research infrastructures such at the Monash Antibody Technology Facility, supported through BPA, not only provides tools and reagents for research but acts as a portal for industry engagement, evidenced by the recent partnership with Pfizer. Our network significantly supports multinational companies such as CSL (Bio21, AGRF) indicative of scale and quality but critically supports Australia’s growing SME community with over 75% of industry partners coming from this sector.

Innovation stems from quality research infrastructure

Australia should aspire to do more than buy in research infrastructure. Understanding the utility, operation, constraints and opportunities inherent in technology ensures research infrastructure centres are ideally placed to contribute to technology development, manufacturing and support. Australia has a long history of such endeavour – Varian and SGE being two such examples in the ‘omics space. BPA is a collaborator to the ARC Centre for Nano-Biophotonics with the aspiration of developing new analytical componentry and validating these in real world research environments.

The understanding of systems through analytical capacities and bioinformatics models is critical for understanding human health, treatment of infectious disease, maximising agricultural productivity and delivering alternative energy supplies through metabolic engineering and genome scale modelling. The extension of these models to application is Synthetic Biology, including the design of genetic componentry, engineering of cellular function and monitoring of activity. A Genome Foundry aimed at automated genome synthesis would increase throughput and uptake of systems learnings in applied settings. BPA activity invests in Synthetic Biology with Macquarie University, UQ and CSIRO. The analytical capacities already offered are necessary for Genome Foundry success.

<u>Strategic benefit lies at the junctures of capabilities</u>

These linkages provide strategic opportunities at the junctures of the Capabilities described in the issues paper, for instance the juxtaposition of environmental sustainability and agricultural productivity; or the interrelationship of food quality with health and medical science. ’Omics infrastructure bridges these junctures providing significant strategic and national value that is otherwise not readily captured.

<u>Cross capability linkages are critical</u>

Science cannot be siloed if it is to be effective. Specifically the value in biomolecular capability is maximised with extension of data interpretation to describe the phenotype. Many NCRIS capabilities have deep understanding of phenotypic measurement.

National benefit from the NCRIS investment is significantly enhanced when relevant capabilities are deployed in an alignment to address collective challenges. BPA has a track record of providing the conduit through which strategic interactions with other NCRIS capabilities have been fostered including coordination of eResearch capabilities (RDS, NeCTAR, ANDS, NCI); structured collaboration with the Australian Phenomics Network, IMOS and TERN; data publication through the Atlas of Living Australia; and conjoint support of a Centre of Excellence with ANFF.

<u>High performing capability exists</u>

BPA is committed to supporting the Australian life sciences community, through a diverse access program, by provision of specific infrastructure requirements and making integrated capability available to initiatives of breadth, scale and complexity in a way that is not readily achievable through other Australian mechanisms. More than 4500 collaborators were supported in 2014/15, of which 15% were focused on industrial and commercial research communities. A focus on meeting broad based demand and strategic deployment to nationally significant programmes in health, agriculture and environmental sectors correlates with Australian opportunities, strengths and needs.

Genomics constitutes approximately 50% of total NCRIS investment via BPA, representative of the growing importance of genomics to biological research and application. The ability to undertake genomics at scale and depth must be balanced with the ability extract meaningful functional value from genomic observation via proteomics, metabolomics and phenomic linkage, all achieved with significant bioinformatics capability. Existing capability is capacity constrained.

<u>Quality governance</u>

National benefit is achievable through the strategic application of investment via mature governance, seeking a balance between strategic deployment of capability to social and economic challenges of national significance, with open access meeting the needs of meritorious researchers and industrial partners.

Maximal value from investment requires the identification of appropriate platform-specific governance structures and facility leaders with the attributes required to lead highly effective teams within their respective research fields, in line with NCRIS principles, and ensure that research infrastructure platforms are delivering quality science in an accessible format.

The agile not-for-profit governance model employed by BPA, ANFF, Auscope and others has proved highly successful in promoting the dual functions of autonomous engagement at facility level whilst ensuring collaborative deployment of capability to challenges of scale and national importance.

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

Agriculture and Food Security is an explicit omission. Whilst implicitly included in the *Environment and natural resource management* capability. Agriculture and Food Security is a critical Australian industry (> 20% GDP; ~$270 billion pa; ~20% GDP; 1.6 million employees, with 57% rural-based) and represents a significant national scientific agenda, across many research organisations including CSIRO, Universities, State Government DPI's, Research and Development Corporations and Industry. This capability should be explicitly added to the *Environment and natural resource management* capability.

Core Capabilities versus "Applied Capabilities"

Within many of the capability areas described in the issue paper, there is description of

- Capabilities that could be considered core research infrastructure, and
- Applied capabilities that apply these core capabilities to thematic areas.

Recognition of core capabilities would strengthen the paper and models could be explored where core capabilities are applied strategically to achieve the aspiration of the roadmap themes, and at the junctures of described capability areas.

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

Independence should be considered as an additional characteristic of governance, especially for networked capabilities where potential conflict in funding allocations may cause tension.

National Benefit should be considered as an additional characteristic of governance, ensuring local investments are externalised to all scientific endeavour that might benefit from access.

Flexibility in governance models should be encouraged to ensure the value individual capabilities are maximised.

The governance criteria are otherwise well defined.

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

Yes. Within the biomolecular capabilities, extension to international facilities has led to significant development of core capability and expertise, for example BPA partnership with EMBL Australia has provided privileged access to EMBL European Bioinformatics Institute and resulted in a local training programme that has now provided world leading skills development for more than 1000 Australian researchers. . Similarly, access to large scale physical infrastructure that is essential to Australia's research priorities but would unnecessarily delay implementation due to a lack of resources/technical expertise should be targets for international access arrangements.

Furthermore, negotiated international access and involvement in international initiatives has fostered Australian involvement a number of significant international collaboration that otherwise would not have occurred. For example, Australia's involvement in the International Cancer Genome Consortium, Australia's involvement in the International Wheat Genome Consortium and Australia's involvement in the Earth Microbiome Project. Each of these has brought national benefit beyond what might have been achieved by individual researcher involvement.

It should be noted that Australian local investment is often required to maximise the opportunity provided through international subscription, providing a virtuous circle of value and efficiency.

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

Where the scale of investment is disproportionate to Australia's ability to fund or utilise.

Where involvement within international research communities is in itself a critical outcome.

Where significant expertise is required that is not readily available within Australia.

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

Yes. Research Infrastructure becomes capability when paired with workforce skills, becoming value adding assets. NCRIS has conventionally supported whole capabilities – hardware, supporting expertise, maintenance and other operational expenses, ensuring capabilities can then be applied to research agendas both big and small. Further, workforce development provides long term strategic value within and beyond the immediate delivery of research capability, including the provision of a translational continuum to industry and career path opportunities not readily available elsewhere in the innovation system.

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

Research Infrastructure and capability are perfect vehicles for supporting training and skills, ranging from early career through to professional development. The following characteristics could be leveraged to maximise training and skills development

- The medium to long term time timeframes over which capabilities are supported provides confidence to build training pipelines that will be used over 5 to 10 years.
- Capabilities are often embedded within educational institutions such as universities and medical research institutes that have the scholarship, accreditation and administrative frameworks to develop and oversee training and skills development.
- The national reach of the capabilities ensures that audiences beyond the host institutions can benefit from education and skills development, extending not only the operation but application of research infrastructures to the broader innovation system.
- Training supports significant national benefit in the translational continuum.

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

Research institutions should see it not as a responsibility (although it is) but as an opportunity. Research infrastructure provides a strategic interface (and shop front) with many different audiences and training is a path by which value can be easily imparted to many communities and individuals, including those from industry.

Further, the depth of understanding of the institutions in learning (training and research) lends itself to valuable co-investment where training should be seen as a critical contribution made by these organisations.

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

The access principles outlined in the issues paper are appropriate. Equal rights for collaborators external to host organisations ensure a culture of open sharing maximises the value of the asset. Meritorious (Category 1 and 2 grant winners) access should be prioritised if capacity is limited.

It should be noted that access can come in many forms – usage of hardware, adoption of methods and techniques, access to data resources and provision of knowhow and advice, all generated from well-run research infrastructures.

There is an opportunity to innovatively consider access models ranging from fee-for-service, to strategically deployed access for research of national significance. This ensures the correct balance between investigator driven research and the availability of capacity for national benefit.

BPA has achieved this through a mixed offering of fee-for-service, targeted access for national collaborative peer reviewed programs such as partnership with ARC COEs, CRCs, CSIRO flagships, NHMRC programme grants and access support for thematic research and innovation in areas of uniquely national interest such as Melanoma biology, Great Barrier Reef characterisation and koala protection.

Commitment to the access principles should be measured to ensure hosts and operators are accountable for upholding the collaborative intent of the programme.

Merit Access

Researchers work to accumulate merit through publications, research track record, reputation and scientifically solid proposals. In many instances Merit is *spent* at the time of application to gain access to national research infrastructure elements.

Different merit allocation processes used by each national research infrastructure element. The result is duplication, inefficiency, waste and a significant source of friction for researchers who need to navigate distinct merit allocation processes for Cloud, Data and HPC.

A merit allocation strategy should:

- Be national to address issues caused by current policies of state based appeasement;
- Aim to be inclusive of all research domains and not just those that require significant computational and/or storage requirements;
- Promote and encourage dynamic use of resources with an end to policies;
- Cater for a wide range of research usage patterns and use cases such as access over a defined period, supporting uptake by disciplines such as social sciences, arts and humanities;
- Articulate and communicate transparent processes; and
- Promote collaboration, sharing and exchange of knowledge and expertise.

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

Defunding and decommissioning are both reasonable expectations as priorities change, the nature of infrastructures evolve or performance is not as required.

Review of capabilities on a predictable basis – 5 year funding cycles with three year reviews focusing on need and performance, will provide the opportunity for 5 year renewal and long term planning, and/or wind down provisions implemented in a rational manner.

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

Research infrastructure and capability is a strategic investment, recognising a variety of requirements including large capital costs, potential for significant duplication and need to connect disparate research communities. However, most importantly is the opportunity for Australia to deploy capability and scale to research agendas that are broad and deep, often requiring approaches on multiple fronts and engagement with researchers from many organisations and disciplines.

The investment in capability is more important than the investment in capital. Indeed in many capabilities the capital can be in part or full met by local organisations or jurisdictions. The ability to sustainably operate this infrastructure in a manner that can allow strategic deployment is not readily sustainable and requires ongoing Commonwealth support.

A model for investment may include

- Capital and maintenance needs met by local, jurisdictional, grant, philanthropic and strategic Commonwealth investment.
- Commonwealth support for skilled operators to promote external access. Co-investment for local or specific research purpose access arrangements are readily leveraged. Zero, partial or full cost recovery from accessing researchers and communities to meet direct costs of operation.
- State jurisdictions may leverage Commonwealth investment to support state based skills, tailored to local industry needs.
- Other dimensions such as subscription from affiliated research communities and industry partners should be considered on a case by case basis, including collaborative opportunities with technology vendors.
- Investment in international subscription for research infrastructure access.
- There is scope for Public Private Partnerships (PPP) whereby the objectives of relevant private enterprise are augmented with public investment to ensure accessibility to existing capability and expertise. BPA has 2 such examples of successful PPP models.

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

Capabilities should aspire to meet international standards and/or accreditation requirements, including in some instance regulatory standards such as those governed by NATA.

Research (and by extension research infrastructure) is not isolated from the continuum through to product development or policy implementation and to ensure work performed today is of value tomorrow (often to unknown communities and questions) work should be performed beneath an umbrella of transparent standards.

The specific nature of standards and accreditations will need to be reviewed on a case by case basis, given the breadth of research capabilities and communities they engage with. The differentiation of research application from clinical adoption should be considered.

For instance, BPA supports facilities such as the AWRI directly involved with analysing food and beverage quality and character – the regulatory needs of this industry differ materially from those supported by other BPA such as the Garvan/Kinghorn genomics centre largely focused on human disease. Both of these facilities hold relevant regulatory approvals but obviously require different accreditation and oversight.

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

Australia's NCRIS model has been studied extensively by international organisations (ESFRI-Europe, NIH-US) and Australia is largely considered ahead of the curve in setting priorities, devising national solutions and fostering a culture of shared access.

Specific capabilities should be considered in the context of international models. For instance, BPA, with the leadership of Dr Susan Pond, has undertaken a strategic planning exercise and there are international models that could be studied (eg. Genome Canada) to ensure strong linkage between research infrastructure provision and application. The current NCRIS model in the area for which we have responsibility has aspired to this and succeed significantly through a fused access model of responding to market need on one hand, and deploying the national asset to prioritised challenges through a big data approach on the other.

Models for best practice implementation and operation should be undertaken on a <u>case by case basis, but not overlooking the excellent operations already established in Australia</u>, often further advanced than their international peers.

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

The diversity of national research infrastructures permits flexibility in funding models from capability to capability. Significant opportunity exists in the 'omics sector for

- Institutional co-investment, aligned with local research need and expertise
- Jurisdictional co-investment aligned with State research priorities and expertise
- Private co-investment in the form of operational partnerships or access subscriptions
- Philanthropic investment in areas of interest
- Significant value adding partnerships with technology vendors
- Investment might support capital acquisition
- Investment might support capital lease, that has a variety of advantages including
    - Amortisation of costs
    - Minimisation of obsolescence
    - Incorporation of warranties and maintenance costs into upfront negotiated financial arrangements.

The correct balance between strategic national investment for national benefit and location of facilities demanded by co-investors should be considered to ensure national priorities are not skewed.

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?

<u>Emerging Directions</u>

General Comments

In all areas of science, new technologies and sensors are driving unprecedented growth in the quality, quantity, diversity, complexity and visualisation of data. The similarly unparalleled growth in data science and machine learning methods are enabling fundamentally new approaches to scientific discovery and regulation of interconnected systems.

In the life sciences, breakthroughs in high-throughput technologies are enabling detailed investigation of cellular components and interactions at the molecular level through to the organismal level (systems biology). These include technologies to generate data on the variation and regulation of the genome, transcriptome, epigenome, proteome and metabolome, connected to phenomic observation.

The application of these molecular approaches is illuminating the intricacies of living matter across widely different scales, from the molecule to the cell to the patient, from the organism to the biosphere.

These advances will not be achievable without cutting-edge research infrastructure together with bioinformatics expertise to undertake coherent analysis of the massive data sets that are generated.

Health Focus

The Issues Paper addressed Health and Medical Science from predominantly a perspective of disease. Opportunity exists to consider health and wellbeing more holistically. The role of food quality on health and wellbeing is understated, for example allergies, obesity, diabetes – all diet-related non-communicable diseases and are the fastest growing cost area of health budgets. The field of microbiomes has exploded in recent years, with implications to immunology, cancer treatment and obesity.

Precision Medicine

Precision Medicine is happening. Personalised or precision medicine will become the paradigm of future healthcare as advances in the ability to perform rapid turnaround genomic and molecular profiling become mainstream in clinical practice. It takes many forms but collectively precision medicine will

- speed up disease diagnoses,
- refine clinical trials to increase success, reducing market costs of drugs,
- improve patient care,
- make available old and new therapeutic interventions,
- allow clinicians to tailor combinations of approaches to simultaneously increase effectiveness and reduce side effects,
- minimise diet-related detrimental impacts on wellbeing through real-time readouts of effects on metabolism
- ensure the health system can sustainably meet ever increasing economic pressures.

To realise the potential of precision medicine significant on going investment in core research infrastructure and capability is required, notably in high quality (accredited) and high throughput (scale) human genomics sequencing capability. BPA (currently NCRIS funded) supports significant capacity at the John Curtin School of Medical Research, Garvan Institute, AGRF and Ramaciotti Centre (UNSW).

<u>The critical genome sequencing infrastructure and sophisticated pipelines required by the state-based health systems to develop precision medicine are and will be accessed through BPA facilities</u>. The centralisation of effort permits efficiencies in scale, harmonisation in approach, standardisation of methods, minimisation of duplication and the environment in which collaboration within and between initiatives is encouraged.

BPA’s network underpins the many national (NHMRC Australian Genome Health Alliance) and State Government (NSW, Victoria, and the ACT), health initiatives: the Melbourne Genome Health Alliance, the ACT Health Genomics Initiative and the NSW Genomics Collaborative.

The adoption of Precision medicine will result from and contribute to a virtuous circle of activity in genomic studies of research cohorts and biobanks, population genomics and big data analysis in context of population health data.

It is arguable that the needs of procession medicine, once embedded tightly within health services, will be met via professional providers such as the recently established genome.one, a spin out from the Garvan Kinghorn centre, supported by NCRIS.

Missing Biomedical Endeavours

The paper discusses at length some desirable new capabilities but overlooks commentary on capability needs to support existing significant endeavour in areas including

- infectious disease including emerging tropical diseases and parsitology
- microbiology – that extends across health, agriculture, environment and industry
- immunology
- neuroscience
- cancer
- indigenous health and well being
- metabolic disorders

Many “core capabilities” including the ’Omics support the full breadth of these significant Australian research needs.

Research Infrastructure Capabilities

We support the inclusion of ‘Omics (5.2.3) as a capability need. ‘Omics must contain dedicated provision for enhanced bioinformatics support. The data explosion in ‘Omics capability can only be exploited appropriately with properly resourced bioinformatics expertise and capability. Significant planning has been undertaken and a community consensus reached on how to effectively deliver bioinformatics capability through a merger of strategically allocated eResearch capacity and specialised bioinformatics capabilities aligned with national science priorities.

‘Omics has a considerably higher uptake and potential than that described in the issues paper and adoption of large scale biomolecular screening technologies pertains to a broader value than that outlined. Through NCRIS, BPA supports significant ‘Omics capacity in Australia – over 4700 users in 2015/16 of which approximately 60% were from the biomedical sector, with geographic access spread on approximately a per capita basis. Personalised or precision medicine is but one dimension of the health and medical research sector enabled by BPA, with significant collaborative and service work in support of a diversity of applications including derivation of mechanisms of microbial antibiotic resistance, characterisation of stem cell lineages, support of clinical trials with biomarker studies, characterisation of biotech products from commercial development pipelines, investigation of viral pathogenesis and treatment, the interaction of food quality with human health and characterisation of cancer malignancy and response to treatment as shadowed in the recent Cancer Moonshot MoU announced by VP Jo Biden on his visit to Australia. This MoU was funded in part by NSW State Government and has fostered a deep collaboration in proteo-genomics characterisation of cancer patient tumours and response to treatment using NCRIS established and operated research infrastructure.

‘Omics extends beyond genomics and includes the measurement of proteins, profiling of metabolites, observation of phenotypic change and in many instances, integration of these disciplines to holistically understand systems.

The provision of the totality of biomolecular needs provides the opportunity for diagnosing health status and disease, developing therapeutic interventions, drug discovery and design, characterisation of biopharmaceuticals and monoclonal antibodies and the monitoring of patients and their response to intervention.

Provision of genome sequencing, mass spectrometry and monoclonal antibody services are but some examples of the capability already offered to the Australian research community. None of this can occur without significant resourcing of bioinformatics – data storage and curation, compute power, development of tools and workflows and access to analytical services is necessary.

Bioinformatics is an inextricable element in ‘Omics investment, required for all aspects of related science including experimental deign, data acquisition and quality measurement, primary and secondary analyses, data curation, contextual analysis, visualisation and publication. Multidisciplinary teams are required to meet the standards required to be internationally competitive, with access to mushrooming data storage, computational power at both the HPC and cloud levels, data curation skills and visualisation capability. Access to international reference data is critical to all analyses.

The ‘Omics collectively, together with affiliated capability in imaging, population health research, biologicals, translational infrastructures and models of disease, will provide opportunities for discovery, translation of discovery into diagnostics and prognostics and ultimately provide the therapies for personalised intervention.

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 should continue to support capability and capacity that enables a contribution to and cooperation with international research infrastructure initiatives. Having significant capacities that can be strategically deployed to support international initiatives, but with significant Australian benefit ensures investment is leveraged against global reach and scale.

National scale permits meaningful international engagement and differentiates NCRIS investment from siloed institutional facilities.

- Australian 'omics research infrastructure facilities are already participants or partners in international initiatives (such as the European Molecular Biology Laboratory (EMBL), ELIXIR, Earth Microbiome, the Human Protein Atlas (HLA) Project, the ProteomeXchange Consortium, and EMBL's Coordination of Standards in Metabolomics). International Cancer Genomics Consortium, FANTOM (functional annotation of the mammalian genome). These programmes provide access to global scale, international standards and research collaborations not possible if operating in local siloes.
- Australia should undertake biomolecular studies at internationally competitive scale in areas of national importance. A recent Cancer Moonshot MoU announced by Vice-President Jo Biden (funded in part by NSW State Government) fostered a deep collaboration in proteo-genomics characterisation of cancer patient tumours and response to treatment using NCRIS established and operated research infrastructure. The programme aspires to analyse 70,000 specimens, to provide insights into molecular behaviour and response in cancer development and treatment, providing ultimately the signatures that clinicians will use on personalised basis when treating patients. Better care at a cheaper price will result.
- Australia should meaningfully cooperate with large international human genomics initiatives such as Genome England, the Global Alliance for Genomics and Health and the recently announced Obama plan to sequence 1 million Americans in support of precision medicine. The national infrastructure capability is well positioned to enable Australia's contribution to such initiatives such as the Cancer Moonshot referred above that Bioplatforms Australia and partners recently signed an MoU with. International cooperation allows Australia to operate at a scale not permissible locally, thereby providing opportunity for scientific and medical inference at global scale.
- Australia is well positioned to undertake more programmes like these, using pre-existing and accessible capability, such as that developed under NCRIS by BPA. <u>The existing network is capacity constrained with a need for additional capital capacity and at least constant operational investment.</u>

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?

Almost all areas of health and medical science (and environment, agriculture, food security and biosecurity) are underpinned by 'Omics science, inclusive of bioinformatics – from discovery through to patient monitoring. The Issues Paper outlines current, emerging and desirable new capabilities, including Biologics, Novel therapies, Biobanking and population genomics, Imaging, Indigenous research, Bioengineering, Stem Cell therapies and managing and leveraging research data insights.

<u>All of these are underpinned or augmented by 'Omics capability</u> and this should be acknowledged within the Roadmap. Indeed existing activity substantially supports many of these dimensions.

There is significant existing capacity within the Australian system supported by NCRIS that has proven highly successful in providing scale and quality, changing culture to one of collaboration and cooperation, creatively deploying capability to significant Australian research and innovation agendas, partnering closely with other NCRIS capabilities and ensuring maximum access to the national investment. Prioritisation of key existing capability should not be overlooked.

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?

Food security and agriculture should be provided separately and explicitly and also requires a more detailed focus within the *Environment and Natural Resource Management* capability. Significant national interests, research depth and existing capability supports food security and agricultural research including biomolecular analysis of food security (biotic and abiotic stress) and quality at BPA, large scale phenotyping at the Australian Plant Phenomics Facility, and a number of COEs and CRCs focused on maximising Australia's potential from the sector.

The importance of food security and agriculture extends into human health and well-being on one hand and environmental sustainability and biosecurity on another. These junctures are significant opportunities.

Biodiversity and Conservation – Australia is a "megadiverse" country. The continent and its surrounding waters are home to nearly 10% of the Earth's species that have evolved independently for the last 30 million years. This rich and unique biological diversity underpins our national well-being through provision of ecosystem services (e.g. carbon cycling, water filtration). It is also a significant source of genetic resources (e.g. soil and water microbes, unique flora and fauna), novel processes (e.g. algal biochemistry) and materials (e.g. eucalypt oils) for industry. In addition, Australia's spectacular natural ecosystems (e.g. the World Heritage Areas of Great Barrier Reef and the Daintree Rainforest) form the basis of an $85 billion tourism industry.

Science teams across Australia's innovation system are engaged in a wide range of research aimed at exploring, exploiting and managing our biodiversity to develop new industries, identify biosecurity threats, conserve rare and threatened species, and maintain a resilient natural environment in the face of rapidly growing pressures from population growth, shifting agricultural zones and environmental change.

Over the last decade, we have sought to move away from "single species" studies and solutions to systems level analyses and actions.

The new science of genomics has transformed agriculture and medicine, providing powerful new research tools and delivering significant opportunities for industry and improvements in human health. The newly emerging science of Environmental genomics now presents the opportunity to similarly revolutionise environmental research.

Evolving rapidly at the interface of next-generation DNA sequencing, evolutionary biology, big data informatics and simulation science, this new discipline is transforming our ability to understand the origins, diversity and dynamics of complex biological systems through very large-scale analyses of the genetic basis of the variation observed within and between species. The meet the potential, research capability inclusive of genomics and more broadly 'omics capacities are required. It will allow us: to measure and identify evolutionary hotspots across our continent; to assess the functional diversity of cryptic ecological groups such as microbial communities; to understand the genetic basis of adaptive traits such as drought tolerance and; to explore the biochemical pathways that underpin potentially valuable traits for industry.

The ’omics are an underpinning capability with relevance for all described capabilities and should be included in Section 10.

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

It is critical that Australia partner into international endeavours, both as a contributor of unique data and beneficiary of the global body of work that comes from being an active participant.

There are many international initiatives across global agriculture, and horticultural crops, environmental surveys and conservation efforts. The NCRIS investment in ‘omics has permitted a rational participation of the Australian research community in a large number of international initiatives including

- International Wheat Genome Sequencing Consortium
- Earth Microbiome – global analysis of microbial biodiversity
- Partnership with the Smithsonian
- Partnership with the British Museum
- 1000 Insect Transcriptome Project
- 10,000 Birds Genome Project
- Genome 10K

National scale – both in geographic surveying and also biomolecular capacity permits meaningful international engagement and differentiates NCRIS investment from siloed institutional facilities. These existing critical collaborations will fall apart without maintaining current investments, and there are other beneficial collaborations that we could be involved in with new targeted investment.

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?

Linkages with other Capability areas are critical, providing the innovative junctures for new research, product development and commercialisation. For instance, capability supported by ANFF has been partnered with that provided with BPA (‘omics) through the ARC Centre for Nano-Bio Photonics to provide new detection capabilities for medical systems.

Linkages with potential new investments in capability such as NMR that has significant value with the ‘omics capability, could be planned and implemented with cohesion.

BPA has worked extensively in both education and training and industrial application of bioinformatics with the Australian Mathematical Sciences Institute (AMSI) to promote the value of mathematics and statistics to modern biology.

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?

<u>Natural History Collections</u>

Australia’s biodiversity is unique and of interest to the rest of the world. Only seventeen 'megadiversity' countries - countries with extraordinarily high levels of biodiversity - are recognised on Earth (Conservation International, 1998). These countries collectively hold around two thirds of the world's biodiversity. Australia is one of these countries. We have more species of native mammals than any other country - one twentieth of the world's mammal species occur only in Australia.

Our natural history collections such as those stored and accessed in our Museums and Biological Collections provide an insight into the breadth and historic makeup of our flora and fauna, including

- Insects
- Herbaria (plants and fungi)
- Mammals
- Fish
- Birds
- Seedbanks

The 'Omics provides a critical discovery tool that will facilitate the exploitation of the potential stored within these collections, providing insights into the genome pools of breeding populations, knowledge on why species succeed or are on the brink of extinction and support the sustainability of critical industries such as fisheries or agriculture.

Characterisation of these collections using 'Omics provides significant opportunities for international collaboration as a result of the unique species and evolution represented in our collections; the Australian specimens held in museums and collections around the world; and the substantial global interest in developing 'Omics analysis techniques for collections samples.

Critically, the natural history collections provide portals for the public to engage with our nation's rich biodiversity and engage with leading edge scientific endeavour.

<u>Indigenous Heritage and Health</u>

The National Centre of Indigenous Genomics (NCIG) supported via NCRIS BPA investment in genome sequencing and bioinformatics, aims to establish a national resource, under indigenous governance, for appropriate and respectful genetic and genomic research that will benefit indigenous Australians. Links with cultural centres to ensure data can be interpreted within a broad context is critical. The ethical constructs being developed will both inform and contribute to the broader indigenous research agenda.

Strategic investment also permits us to close the loop on such a cultural study with precision medicine, ensuring personalised data can be used for maximal community benefit.

National Security

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

<u>Biosecurity</u>

Biosecurity needs to be considered as part of any national security strategy.

The 'Omics significantly support biosecurity research, development and surveillance including emerging disease threats, zoonotic incursions, protection of agricultural and horticultural crops from biotic stresses such as rust, and characterisation of wildlife disease.

BPA has extensive collaborative activities with AAHL, state based Departments of Primary Industries, zoos and aquaria, herbaria and museums and human infectious diseases units such as the Melbourne based infectious Disease Reference Laboratory.

Omics technologies and informatics are vital to integrate data/reports and interpretations or treatments as soon as potential pathogen incursions are encountered on a farm or forestry plot:

capturing in real-time, elements of the incursion, sampling/survey, diagnostics, remedial treatments and field/laboratory work leading to the development of new cultivars or multiple disease resistance.

In this regard, BPA has extensive collaborative activities with CRCs and universities that are involved in delivering appropriate research infrastructure in support of a biosecurity framework. The exemplar project has been instrumental in changing Department of Agriculture policy to now embrace next generation sequencing technologies as part of routine diagnostics.

The breadth of national value of ‘omics capability should be recognised in the underpinning research infrastructure section of the Issues Paper.

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?

<u>The ‘omics are a truly underpinning capability</u> that are now used in almost every aspect of biological research, be that of discovery in cell biology, characterisation of organisms and their interaction with their environment, ecological surveys, understanding of human health and disease that impacts on it. This could be reflected in the issues paper with a description of the ‘omics within Section 10, *Underpinning Research Infrastructure.* The table below illustrates the breadth and depth of ‘omics, defined as genomics, proteomics and metabolomicsto the national research and innovation system.

	Basic Research	Translational Research	End User
Human Health and Well Being	Gen, Prot, Met	Gen, Prot, Met	Gen, Prot, Met
Agriculture and Food Security	Gen, Prot, Met	Gen, Prot, Met	Gen, Prot, Met
Natural Resources (Environmental Science, Biodiversity Conservation, Energy, Mining)	Gen, Prot, Met	Gen, Prot, Met	Gen, Prot, Met
National Security (Biosecurity)	Gen, Prot, Met	Gen, Prot, Met	Gen, Prot, Met
Cultures and Communities	Gen, Prot, Met	Gen, Prot, Met	Gen, Prot, Met
Industrial Application	Gen, Prot, Met	Gen, Prot, Met	Gen, Prot, Met

The needs of HPC, high capacity networks, access and authentication are all required within the life science communities, especially for ‘omics enabled science.

Strategic allocations for high demand need such as human whole genome sequencing would be nationally valuable, ensuring adherence to best practice standards, sharing of data at scale and throughput matching the sequencing throughput within genomics laboratories such as Garvan/Kinghorn. Many state and Commonwealth (NHMRC) genomics health alliances are utilising the existing capacity at NCI (supported by BPA NCRIS investment) and this demand will only grow.

Significant second tier or shoulder scale HPC is delivered for the ‘omics including capacity at Intersect, VLSCI and MASSIVE. Links to peak capacity could be considered.

Collaborative development and deployment of dedicated HPC capacity for strategic national programmes would be beneficial.

<u>Security</u>

As the Australian research community has become increasingly dependent on national research infrastructure, it is critical to consider the security requirements of the platform. High profile incidents[1] have shown that foreign state based agencies are targeting Australian research assets. The

[1] http://www.abc.net.au/news/2015-12-02/china-blamed-for-cyber-attack-on-bureau-of-meteorology/6993278

reliance on Internet based systems by Australian researchers and the targeting of Australian research assets by foreign governments justifies a more considered and coordinated approach than the current arrangements.

The Australian eResearch capability should develop an overall security strategy that reflects the importance of the platform to Australian researchers and the sophisticated nature of external threats. This strategy should be developed with input from external expert agencies that have considered these issues over a long period of time and have developed robust strategies such as the Australian Signals Directorate[2].

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?

The identified capabilities and directions are well described.

Added emphasis on the strategic and integrated allocation of resources (differing computational needs, storage types etc.) to prioritised capabilities would be of national value, benefiting large communities of researchers involved in both large scale activities and smaller investigator lead research.

BPA has worked closely with RDS, NeCTAR, ANDS and NCI and made significant improvements to the data system for the Life Sciences and there is a developed consensus view of strategic provision of national resources.

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

Australia should consider joining ELIXIR, a pan-European e-infrastructure network who's Hub is located alongside EMBL-EBI (UK) and with Nodes in centres of excellence for bioinformatics across Europe. The collective will provide compute and storage on a previously unprecedented scale. Biological and medical data of many different types will be integrated and made available on an open access platform with tools and standards created to enable maximum benefit to be derived from users around the world.

ELIXIR represents the future of life science data, capture, storage and delivery. In recent years bioinformatics has come to the fore as a vital new discipline, providing solutions to the challenge of managing ever greater volumes of research data. ELIXIR has emerged as the only viable solution for the collective European management of data.

Countries that are or will become ELIXIR Member States benefit in the following ways from their participation in this infrastructure:

- Participating in the State of the Art
- Data Integration
- Storage and Compute
- Standards and Ontologies
- Training
- Benefitting from Collective Expertise in Bioinformatics
- Reducing Fragmentation and Aligning National Priorities
- Capacity Building
- Shaping the Direction of ELIXIR

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[2] http://www.asd.gov.au/

- Preserving National Investments in Life Science Research
- Supporting Local Jobs and Growth
- ELIXIR’s Interactions with Industry
- Joint Applications for Additional Funding
- A Stronger Collective Voice

To ensure maximal national benefit from joining ELXIR Australia needs to harmonise the national bioinformatics effort, bringing together strategic allocations of integrated eResearch resources with bioinformatics talent, national projects of scale and contribute to the initiative as a peer. Significant planning and progress has been made by BPA, EMBL ABR and others in preparation of joining ELIXIR.