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2016 National Research Infrastructure Roadmap
Capability Issues Paper
University of Wollongong Response

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Health and Medical Sciences

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

The integration of biomaterials, advanced fabrication and clinical applications of these is a clear emergent area requiring national investment.

A translational facility is needed to support the development of materials, 3 dimensional structures and medical devices resulting from them with suitable good manufacturing practice (GMP) traceability. This capability is essential to support investigations of new materials and structures from them and is essential for advanced bio-fabrication in Australia.

NCRIS facilities should actively engage in the development of emerging regulatory framework discussions, particularly in the bio and nano-domains.

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

Overall, the University of Wollongong (UOW) strongly supports a renewed focus on governance for the national research infrastructure. The proposed key characteristics presented within the Issues Paper represent the foundational requirements of a sound governance model of future investment, operation and oversight.

It is also suggested that "strategic interoperability" be considered as a key principle in the governance model for national research infrastructure. It is regrettable to note that a competitive "market" appears to have been created amongst some of the state-based e-research agencies and such an environment is not conducive to the fair and efficient sharing of national research resources. It is believed that a strong centralised governance model would prove highly valuable in ensuring a well-formed, congruent strategy across institutions, agencies and levels of government.

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

Yes, Australia's national infrastructure will never be able to provide access to every facility needed by researchers. Ideally Australia should be a party to co-investment in such facilities. Paying to access these facilities may provide a favourable economic business case, however, the greatest

benefit to Australian research programs occurs where investigators are active participants in collaborative projects, including the construction, operation and governance of such initiatives.

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

They are inextricably linked. The collaborative research infrastructure roadmap appears sound and well-measured, however, there is a need to further develop workforce skills. One possible solution could be the integration of "e-research" training with RTS-supported Honours and HDR student cohorts. Coursework-integrated PhD and Master degrees could provide an ideal platform for skills development and training delivery.

The NCRIS facilities provide an opportunity to provide training to the next generation workforce. In the case of ANFF (Australian National Fabrication Facility), this includes those required to lead the next generation of advanced manufacturing technologies.

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

NCRIS facilities are playing an increasing role in nationally funded activities such as the ARC Industrial Transformation Research Hubs and Training Centres and CRC-funded research training scholarships. It should assist not only Universities, but also users in the industrial sectors.

These facilities are also used in preparing online education materials, such as the MOOC-produced by the ANFF Materials Node on 3D Bioprinting (see: https://www.futurelearn.com/courses/bioprinting).

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

Within a local context, universities should focus on equipping their departments to produce infrastructure-ready researchers and technical specialists, in a way that involves breaking down internal silos. As an example, at UOW we have researchers in the humanities and arts doing research on film in Asia but also tapping into social media using big data and programming experts in other departments.

UOW has experienced a growing volume of this type of activity and we believe this is a result of the NCRIS program's effectiveness in building capabilities and awareness. There is clearly demand amongst researchers for localised advanced computing and data specialist support and training, however, funding for localised support and development remains an ongoing issue.

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

It is UOW's experience that NCRIS initiatives operating under co-investment funding models appear to provide the most sustainable operating models. It is accepted that NCRIS facilities have required significant taxpayer investment and the historical approach of offering "free" services and resources to researchers cannot be sustained indefinitely. However, there are high levels of dissatisfaction where arbitrarily determined access fees and retrospective cost-recovery policies have been applied by some projects.

To remedy this situation, the investment cases and initial planning processes for NCRIS initiatives require a renewed focus. Co-investment offers the most realistic path to sustainable

research infrastructure and a greater degree clarity on up-front contractual obligation, financial commitment, operational resourcing strategies, and unified governance will ensure greater buy-in and long-term support from end-users and research organisations. In this regard, the NCI's Partner Shares access program represents a highly successful co-investment model that ought to be closely considered by other NCRIS facilities.

Within industry, the ubiquity of cloud computing and storage technology has reached a stage where capacity is now a commodity. With the exception of high-end HPC applications, it is feasible that access to standardised resources could be provided through a public-private partnership model. Commercial cloud IT providers are exceptionally efficient at operating resilient, large-scale infrastructure. In cases where service offerings are commodities and investment does not offer a national strategic advantage, it would be logical to contract out such services rather than task the NCRIS to attempt competing with the commercial sector.

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

Regulatory restrictions (i.e., NICNAS – National Industrial Chemicals Notification and Assessment Scheme) are out of alignment with the development of R&D nanomaterials, e.g., the production of bulk materials for R&D applications is at a workable limit of 100 kg, but when nanomaterials are considered a 100g limit is set. NCRIS needs to be engaged with regulatory bodies in the area of nanomaterials production for academic and industry based R&D developments.

<u>Health and Medical Sciences</u>

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

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?

We believe the following areas are missing capabilities for Health and Medical Sciences:

(i) Structural biology, the discipline that focuses on determining atomic-detailed structures of biomolecular complexes, is undergoing a revolution. In our fight against disease, knowing the structure of the proteins involved is a key requirement for understanding disease mechanisms and the development of drugs. The recent development of cryo-electron microscopy platforms that are able to visualize large biomolecular complexes at a resolution of down to 2 Ångstrom, is enabling biomedical scientists to visualize structures of membrane proteins and large multi-protein complexes, systems of key relevance to disease virtually inaccessible by methods such as X-ray crystallography done at synchrotrons.

The impact of this new technology on Australian science is clear: several institutions have purchased, or are about to purchase, cryo-electron microscopy platforms. There are several financial and logistical challenges associated with purchasing and running these platforms that have direct impact on the ability of Australian biomedical scientists to perform this type of work. As such, we need to think carefully about how these new technologies are integrated into Australia's national research infrastructure framework.

The key challenges are cost and access. The imaging platforms have a purchase price of $5–10 million each and cost ~ $500,000 per year to maintain and operate (service contracts and

technical support). These costs are prohibitively high for individual institutions to purchase their own equipment exclusively for the use of their own researchers. There is a growing appreciation in the field of the need for a model where certain institutions commit to the purchase of the high-end microscopes and allow access to these systems by external researchers. Partner institutions would invest in the lower-end cryo-electron microscopes that support screening of the biological samples to optimise quality before time on the high-end microscope is requested. Such a 'hub-and-spokes' model would allow high-throughput screening of samples at the location where the researchers are and would only demand time on the high-end system for highly optimised samples.

Examples of successful implementation of such a system are the electron BioImaging Centre (eBIC) at the Diamond synchrotron (University of Oxford, UK)[1] and the Netherlands Centre for Electron Nanoscopy (NeCEN) at Leiden University[2], each with two high-end Titan Krios microscopes and the associated support structure to facilitate external users with samples optimised at their home institutions.

In Australia, similar structures are emerging: Monash University purchased a high-end Titan Krios in 2015, with the University of Melbourne in the process of purchasing a screening microscope. In New South Wales, the University of Wollongong (UOW) has recently committed to the purchase of an integrated high-end system (two microscopes), with the nearby Victor Chang Cardiac Research Institute purchasing a screening microscope and UNSW working towards doing the same.

Another critical factor is the broader integration between different hub-and-spokes networks. Downtime of the high-end microscope at one hub caused by maintenance or unexpected malfunction results in large backlogs and needs to be dealt with in a way that optimally makes use of available microscope time elsewhere in the country. Further, ensuring that Australian users have access to the most state-of-the-art equipment requires coordination between institutions to most efficiently use available time at all institutions. Finally, upskilling of technical support personnel can only be efficiently achieved by creating the networks within Australia that allow mobility of personnel amongst institutions.

For example, UOW, in the process of establishing itself as a cryo-EM hub, is in close communication with the existing cryo-EM facility at Monash University, with a clear commitment at both of these institutions for a closer and formal relationship in the future.

In the context of these rapid developments that are dramatically transforming the landscape of structural biology in Australia, UOW believes a strong commitment from the Australian Government is required to support the collaborative networks described here. To ensure the competitiveness of structural biology in Australia to satisfy the growing need for high resolution structures to guide drug discovery and understanding of the biochemical mechanisms of disease, there is also a need for formalisation of support structures that are broadly inclusive and allow all institutions in Australia to benefit maximally.

Previous generation cryo-EM capability currently comes under the umbrella of NCRIS through the Australian Centre for Microscopy & Microanalysis (AMMRF) via its node at the University of Queensland. The Monash facility is not currently associated with AMMRF. AMMRF's capabilities are currently focussed heavily on chemistry and materials science applications of

[1] http://www.diamond.ac.uk/Science/Integrated-facilities/eBIC.html
[2] http://www.necen.nl/

electron microscopy and other high-end analytical instruments, with biological cryo-EM being a relatively minor component.

It is estimated that the total national capital investment in biological cryo-EM will rise to >$60M over the next 2–3 years and will continue to grow after that. Efficient structures to maximise return on this investment need to be developed. They may be better aligned with other high-end facilities for structural biology, where national investment has in recent times been focussed on the macromolecular crystallography and small-angle X-ray scattering beamlines at the Australian Synchrotron. That community also works on a hub-and-spokes model, where sample optimisation occurs at distributed in-house screening facilities prior to collection of highest-quality data at the synchrotron.

The difference is that the cost differential between screening and high-end instrumentation for macromolecular crystallography is much wider than for cryo-EM. For cryo-EM, it does not make sense to have a single national high-end facility. Rather, there will ultimately be multiple hubs that will require coordination of user access to ensure timely generation of highest-quality data.

The process of solving high-resolution biological structures by cryo-EM (both in single-particle reconstruction and electron cryo-tomography) is also very computationally intensive and will generate significant demand on national supercomputer resources and data storage facilities.

To address these issues, consideration should be given to expanding or modifying the current AMMRF structure to support dedicated cryo-EM infrastructure, with a strong connection or alignment with current synchrotron-based structural biology efforts. Such a strategy would: (i) enable the focussed investment and support that cryo-EM as an emerging structural biology tool needs, (ii) optimally benefit from existing experience within our current high-end structural biology facilities, and (iii) leverage the current organisational and governance structures of the AMMRF.

(ii) Medical Devices that require materials development seamlessly integrated with emerging customised fabrication capabilities should be included. Examples of this include sensor systems for medical diagnosis, health monitoring, implantable structures to address clinical challenges such as tissue regeneration and the realisation of neutrally driven prosthetics. The realisation of 3D cell printing is facilitating such developments, as well as providing unprecedented experimental models (e.g. the brain on a bench project) for fundamental exploration into the development and treatment of neural diseases.

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?

The partial vacuum left by CSIRO in climate science would be well served by a national centre with secure support to address long term issues around climate change – not just measurements and climate models, but adaptation and mitigation as well.

Two examples of existing infrastructure serving the environment capability area are the new research ship, the RV Investigator, and TERN (Terrestrial Ecological Research Network). The RVI is only 2 years old and cost > $100M, but is funded for < 100 days at sea a year. As a nation, have a responsibility in remaining the premier research base for Southern Ocean and Antarctic research. Australia is the most advanced country in the southern hemisphere to lead research in

our region, and leverages strong partnerships with northern hemisphere researchers which would suffer mightily if we were to lose these connections. TERN is in a parlous state after much of the CSIRO support and involvement in it has ceased. A continental scale environmental monitoring network is essential.

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?

Key missing capabilities are systems for rapid new materials screening, including integration with the most advanced (probably customised) fabrication methods. These will be crucial for the translation of physics/chemistry and materials science into economic, health and social impacts over the next decade.

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

We recommend the development of an international advanced materials fabrication network, providing Australian researchers with access to global fabrication facilities, similar to the International Synchrotron Access Programme. Australia is well placed to play a leadership role in such a development.

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

We recommend the development of an international network of rapid-prototyping centres across countries focussed on the fabrication of cutting-edge devices and structures for industry.

Enhanced interactions of medical and biomedical capabilities with the materials and advanced fabrication domains will be critical into the future.

Understanding Cultures and Communities

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

We recommend that the Understanding cultures and communities capability area should be broadened to "Understanding and supporting cultures and communities". Effective enablement of collaboration requires a focus beyond just data for research and discoverability. There is a tangible need to also support the software implementations of models and other software and digital infrastructure that enables data to be understood and used by other researchers and community stakeholders. Bundling research publications with *both* data and software assists with scientific replicability but also fosters development of deeper collaborative networks and innovation-focused culture.

National Security

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

There is a clear opportunity for enhanced engagement with other NCRIS capabilities (e.g. ANFF) to address issues of sensing and detection for biosecurity applications.

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?

In many cases, services are becoming commoditised with little differentiation between commercial offering and scarce strategic value in building IT infrastructure from first principles. On this basis, the research infrastructure roadmap should include a renewed focus on services and enabling capabilities.

A clear exception to this case is high performance computing, which still requires large-scale specialised hardware, software and expertise to build and operate. Further, there must be

adequate scope to support developmental investigation and emerging technologies, such as GPU computing, where commercial service offerings do not exist or do not yet provide attractive economic returns.

Good Manufacturing Practice (GMP) facilities for the development of materials for use in the biomedical and bio-devices sector, is a missing national capability. While GMP facilities are available under NCRIS for novel therapy capabilities, such as immunotherapies, there is a gap in the area of the production of materials and subsequent fabrication into structures and devices, under a manufacturing traceabilty framework afforded by GMP, for clinical application. An example of this can be seen at the ANFF Materials Node where bio-scaffold materials such as gelatin methacryloyl (*GelMA*) hydrogels have been produced. However, translation of these materials beyond simplistic animal models into human application is hindered through this missing capability link.

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?

National agencies such as ANDS have been instrumental in raising the awareness of sound research data management and enabling solutions for specific-applications. However, there is a palpable gap in “e-research" skills proficiency amongst researchers. Traditionally activity has focused on researchers with an established degree of comfort ability and competence in working with data. Continual incremental improvements in the basic skills and practices of less-experienced groups have an equally significant impact as large-scale improvements to support high-end users.

Based on UOW’s local experience, there is a clear need for further basic research data skills training and support at Australian universities. In response to local outreach actives, UOW stakeholders have stated the need for such services must be reliable, accessible, relevant and tailored. Respondents to a recent survey on research data management practices at UOW mentioned the importance of:

- Understanding the specific requirements of disciplines and individuals to affect robust data management. This need is particularly pronounced within HASS disciplines and research groups with concentrated levels of commercial and contract research activity.
- An understanding of the local resources available (or not available) to support individual researchers and groups, in addition to the relevant national infrastructure and services.
- The need for accessibility, trust and strong relationships.

With regard to data services and infrastructure, recent activity has been guided by a pronounced emphasis on building technical capability, supporting discoverability and enabling access to research data. A degree of relative maturity has been reached and it is now appropriate to consider re-scoping program priorities to focus on supporting the effective use of the infrastructure and services that have been developed. Agencies such as ANDS perform a vital and truly commendable job in connecting researchers to the various available resources and navigating a complex, changing subject domain, however, there is a requirement for further support and training in the use these resources to ensure the greatest possible value is now realised from earlier investments.