THERAPEUTIC INNOVATION AUSTRALIA

ANNUAL REPORT 2013–14

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Acronyms and abbreviations

ACP	Australian Centre for Pharmacometrics
ACRF	Australian Cancer Research Foundation
AIBN	Australian Institute for Bioengineering and Nanotechnology
ATP	Australian Therapeutic Pipeline
CCB	Centre for Cancer Biology
CCIA	Children's Cancer Institute Australia
CCR	Centre for Clinical Research
CDCO	Centre for Drug Candidate Optimisation
CEO	Chief executive officer
CIPDD	Centre for Integrated Preclinical Drug Development
CTAG	Clinical Trials Action Group
CTBU	Clinical Trials and Biostatistics Unit
EIF	Education Investment Fund
EU	European Union
FICF	Florey Ion Channel Analysis Facility
GVHD	Graft versus host disease
MIMR-PHI	MIMR-PHI Institute of Medical Research
MIPS	Monash Institute of Pharmaceutical Sciences
MoU	Memorandum of Understanding
MSC	Mesenchymal stromal cells
NBF	National Biologics Facility
NCRIS	National Collaborative Research Infrastructure Strategy
NHMRC	National Health and Medical Research Council
PTNA	Paediatric Trials Network Australia
Qld	Queensland
R&D	research and development
SSI	Super Science Initiative
SVI	St Vincent's Institute
TGA	Therapeutic Goods Administration
THD	Translating Health into Discoveries
TIA	Therapeutic Innovation Australia
UQ	The University of Queensland
VCCT	Victorian Consortium for Cell-based Therapies

From the Chairman and CEO

Interest in development of new therapeutics continues to grow with a record investment made in this sector over the last year. Locally, TIA continued its work in supporting this sector through enabling promising Australian medical research discoveries to move from the laboratory bench through to proof of concept testing.

TIAs acknowledges the great work undertaken by its large collaborative network of medical research institutions, universities and hospitals. Collectively this network provides access to 45 capabilities, each providing access to technical expertise and advanced translational research infrastructure. The investment in the network over the year reached $42.1M. This funding has resulted in several substantial outcomes including the generation of twelve patents and five licensing transactions. It is however the development of 67 proof of concept products and 80 clinical trials which best reflect the national significance of our suite of research capabilities. Taking these novel drug candidates further along the development pathway allows Australia to more fully realise the commercial and health impacts of its discovery research investments.

Beyond research and commercialization activities TIA has expanded its local collaborations through the launch of the Australian Therapeutic Pipeline (Pipeline), a national therapeutic product development pathway. This initiative will close the remaining gaps in TIAs consortium; drawing together the critical capabilities required to develop promising small molecule, biopharmaceutical, cell therapy and biomarker technologies. The Pipeline will include infrastructure supporting clinical trials, cGMP manufacture of recombinant proteins and fill and finish capabilities which will enable researchers to more easily convert health technologies from a laboratory bench concept into a bedside reality.

The Pipeline is first for Australia and, to the best of our knowledge, it is the first fully national consortium of its type in the world.

Local connections are vital to lift our innovation productivity but building our international engagement is critical for Australia to remain relevant in global drug development programs. These collaborations have been a feature of the last year with TIA executing MOUs with three European agencies and being a foundation partner in development of a global translational health research consortium, a consortium involving the National Centre for Advancing Translational Sciences (US), The Centre for Drug Research and Development (Canada) and the European Advancing Translational Research in Medicine (Europe). These agreements will support our efforts to improve the efficiency and effectiveness of translational research.

Terry Slater
Chairman

Dr Stewart Hay
Chief Executive Officer

December 2014

Highlights of 2013-2014

A look at Therapeutic Innovation Australia's highlights of 2013–14.

TIA administered nearly **$6 million** dollars of National Collaboration Research Infrastructure Strategy (NCRIS) 2013 funding to 21 participants.

NCRIS 2013 funding will enable a projected **64%** increase in international researcher access to facilities, an **80%** increase in interstate researcher access and a **41%** increase in same-state researcher access.

Facility infrastructure utilisation rates are also expected to increase, from 57% in 2013–14 to **73%** in 2014–15, as a result of NCRIS funding.

TIA is **extending its networks overseas**, by signing numerous memorandums of understanding with influential European Union collaborators, including EU-OPENSCREEN, the European Clinical Research Infrastructure Network and the European Advanced Translational Research Infrastructure in Medicine.

Tomorrow's drug developments will largely include small molecules, biopharmaceuticals and cell-based therapies – technologies all supported by TIA.

TIA has taken the first steps to nationalise the TIA Queensland Node model to create the **world's first** national supply chain.

1. Supporting translational research in Australia

Therapeutic Innovation Australia (TIA) enables the elements of successful pharmaceutical and device development – facilities, people and networks, and projects.

Since 2011, TIA has managed more than $100 million in translational research projects that have encompassed product optimisation, preclinical development and clinical trials, which are key elements in translating the outputs of life sciences discovery research into new products for improving human health and generating economic activity. TIA has played a part in delivering programs and projects such as the NCRIS human cells for transplant project and the 2011 Translating Health into Discovery Part 2 (THD2) project – funded via the Australian Government's Education Investment Fund (EIF). TIA will also help to deliver the NCRIS Translating Health into Discovery (THD) project as part of NCRIS 2013. These programs have seen Australian Government investments of more than $2.4 billion since 2004 into a broad range of research infrastructure across a variety of capabilities, including translational medicine.[1]

TIA complements existing research support organisations, such as the National Health and Medical Research Council (NHMRC) and the Australia Research Council, and addresses the gaps that these capable bodies leave behind. For example, the NHMRC does not fund hard infrastructure; TIA enables access to infrastructure so that research can be translated and commercialised (see Figure 1).

Figure 1: Therapeutic Innovation Australia's place in the Australian clinical research landscape

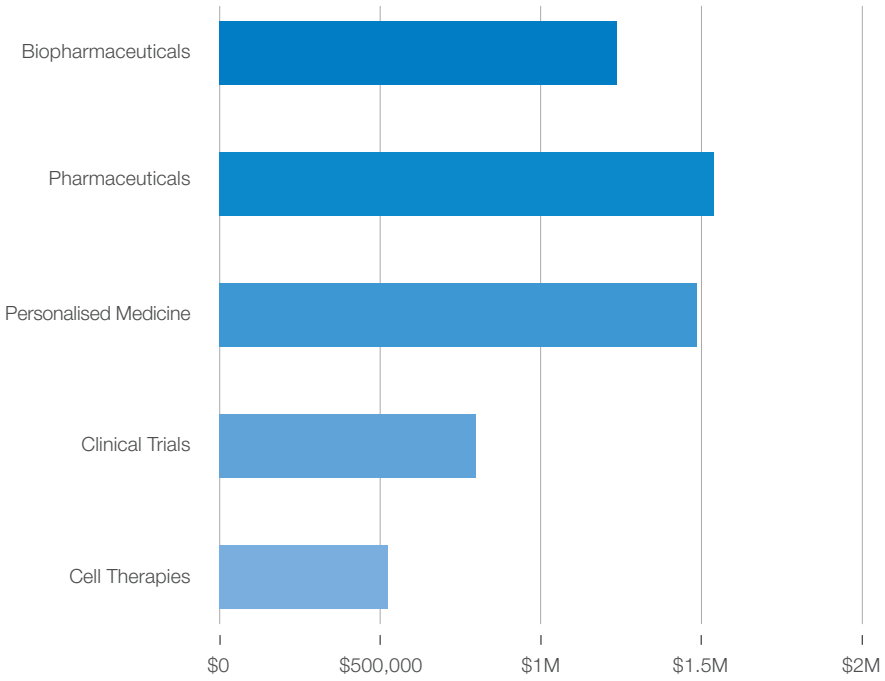
1.1 Collaborating in research infrastructure

The Australian Government Department of Education's NCRIS helps provide Australia's researchers with access to high-quality, operational research infrastructure facilities – that is, NCRIS helps to increase our preclinical capabilities. Translating health research is one of the department's research priorities, to enable individual discoveries to progress. This, in turn, improves patient outcomes and quality of care, and boosts the national economy.

1. www.education.gov.au/national-collaborative-research-infrastructure-strategy-ncris
2. DIISRTE (2011). *National Collaborative Research Infrastructure Strategy strategic roadmap 2011*, DIISRTE, Canberra.

The first NCRIS funding ran from 2009 to 2011 and, due to its success, the strategy was renewed for 2013. TIA awarded nearly $6 million dollars to six different research disciplines in 2013 as a part of NCRIS 2013 (see Figure 2).

Figure 2: NCRIS funding 2013, by discipline



Note: Excludes goods and services tax (GST).

Bipharmaceuticals: CSIRO and the University of Queensland's Australian Institute of Biotechnology and Nanotechnology;

Cell therapies: Royal Perth Hospital's Cell and Tissue Therapies WA, Monash Institute of Medical Research – Prince Henry's Institute, which operates the Victorian Consortium for Cellular Therapies Isolator Facilities Sydney Cell and Gene Therapy, Westmead;

Clinical trials: the University of Sydney NHMRC Clinical Trials Centre's Australian New Zealand Clinical Trials Registry; the Paediatric Trials Network Australia, hosted by the Children's Hospital at Westmead, QIMR Berghofer's Clinical Trials and Biostatistics Unit;

Pharmaceuticals: Monash University's Australian Translational Medicinal Chemistry Facility, and Centre for Drug Candidate Optimisation; the Children's Cancer Institute Australia's ACRF Drug Discovery Centre for Childhood Cancer; Eskitis Institute's Compounds Australia, the Florey Ion Channel Analysis Facility; Walter and Eliza Hall Institute's High-Throughput Chemical Screening Facility, the University of Queensland's Centre for Integrated Preclinical Drug Development/TetraQ;

Personalised medicine: Centre for Cancer Biology (a partnership of SA Pathology and the University of South Australia)'s ACRF Cancer Genomics Facility; Centre for Clinical Research and Diamantina Institute at the University of Queensland, the Garvan Institute's Kinghorn Centre for Clinical Genomics; Melbourne University's Centre for Translational Pathology and Peter MacCallum Cancer Centre's Molecular Pathology Laboratory, Queensland University of Technology's Institute of Health and Biomedical Innovation.

1.2 Moving towards nationalising the TIA Queensland Node

The TIA Queensland Node (the Qld Node) was established using THD 2011 funding and comprises five institutes: The University of Queensland (UQ) Diamantina Institute, UQ Centre for Integrated Preclinical Drug Development (CIPDD) (TetraQ), Queensland University of Technology's Institute of Health and Biomedical Innovation (IHBI), UQ Centre for Clinical Research (CCR), and QIMR Berghofer Medical Research Institute's Clinical Trials and Biostatistics Unit. Officially launched in 2012 as a 'trial network', the successful node represents a model for a national network.

The Qld Node provides access to coordinated and integrated translational health pathways for researchers in different areas.

1.3 Developing the 'drugs of the future'

Biopharmaceuticals, small molecules and cell therapies are rapidly becoming the next thing in pharmaceutical therapy development. TIA supports these therapies through several means, including EIF and NCRIS funding.

1.3.1 Biopharmaceuticals

Biopharmaceuticals and therapeutic proteins produced by recombinant DNA technology are a rapidly growing class of new therapies.

THD 2011 funding was used to establish a National Biologics Facility (NBF) that can produce recombinant proteins from a range of expression systems, and in sufficient quantities and purities to allow researchers to perform preclinical evaluation and protein testing. The NBF is based on the existing infrastructure for protein production at the Australian Institute for Bioengineering and Nanotechnology (AIBN) in Brisbane and CSIRO in Melbourne.

1.3.2 Small molecules

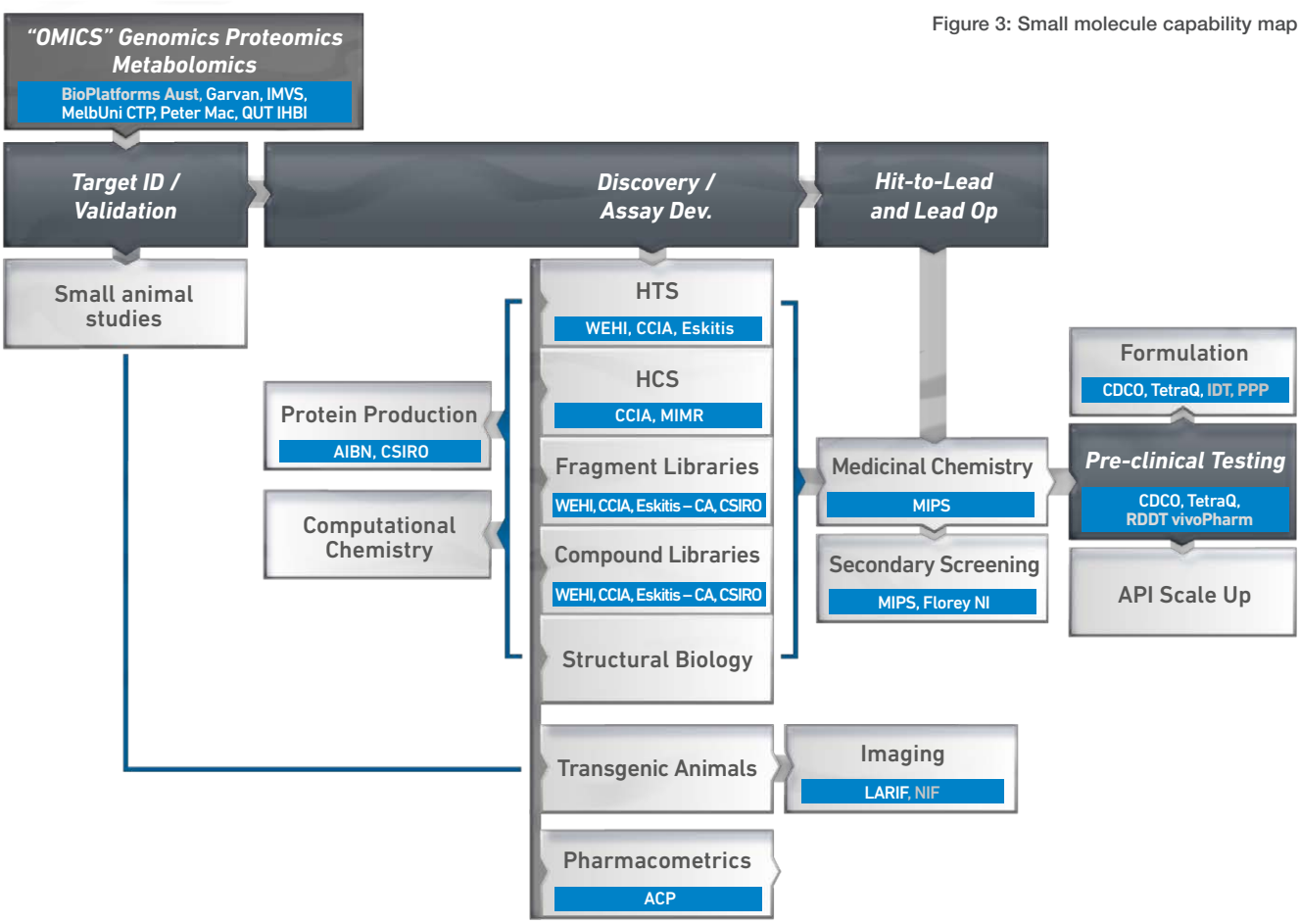
Small molecules are quickly becoming another major area of therapeutic research and trials.

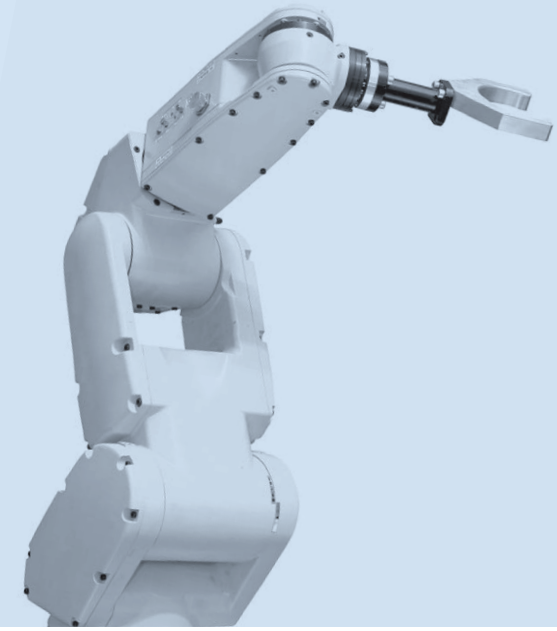
The Monash Institute of Pharmaceutical Sciences (MIPS) aims to address a capability gap in translation medicinal chemistry – a vital component of small molecule synthesis. Translational medicinal chemistry is not well supported by most universities: the infrastructure is not available, the different disciplines are siloed and funding models do not support applied research.

The Centre for Drug Candidate Optimisation (CDCO), as part of MIPS, provides lead optimisation advice and support for emerging drug discovery programs. Drug candidate optimisation is essential for good drug development – it combines medicinal chemistry, biology and pharmaceutical sciences to identify the best drug candidates to progress to the later stages of development.

TIA is a part of the establishment of a broader Virtual Pharma Drug Development Network that will support hit-to-lead and lead optimisation programs, which MIPS is an important part of (see Figure 3). EIF / SSI funding have been instrumental in enabling the construction and fit-out of the Australian Translational Medicinal Chemistry Facility at MIPS to advance these programs.

Figure 3: Small molecule capability map





In the spotlight:

Using small molecules to personalise children's cancer treatments

Small molecules are being used in pilot studies for children with cancer at the Children's Cancer Institute Australia (CCIA). Gene expression profiling of individual cancer patient tumour cells is used to identify key upregulated target genes for which a targeted therapeutic exists. The specific agents are then functionally tested on the patient's cells to determine if overexpression of the specific target protein results in heightened sensitivity to that agent. These approaches will help develop and implement targeted therapeutic approaches and improve the outcomes of children with high-risk and refractory cancer.

Small molecule libraries can be used to profile patient tumours to identify drug targets for which a molecular-targeted drug is available. Modelling and high-throughput library screening of approved and investigational drugs are used to 're-position' clinically approved drugs for use in individual patients whose tumour cells respond to drugs that may not routinely be used for cancer treatment.

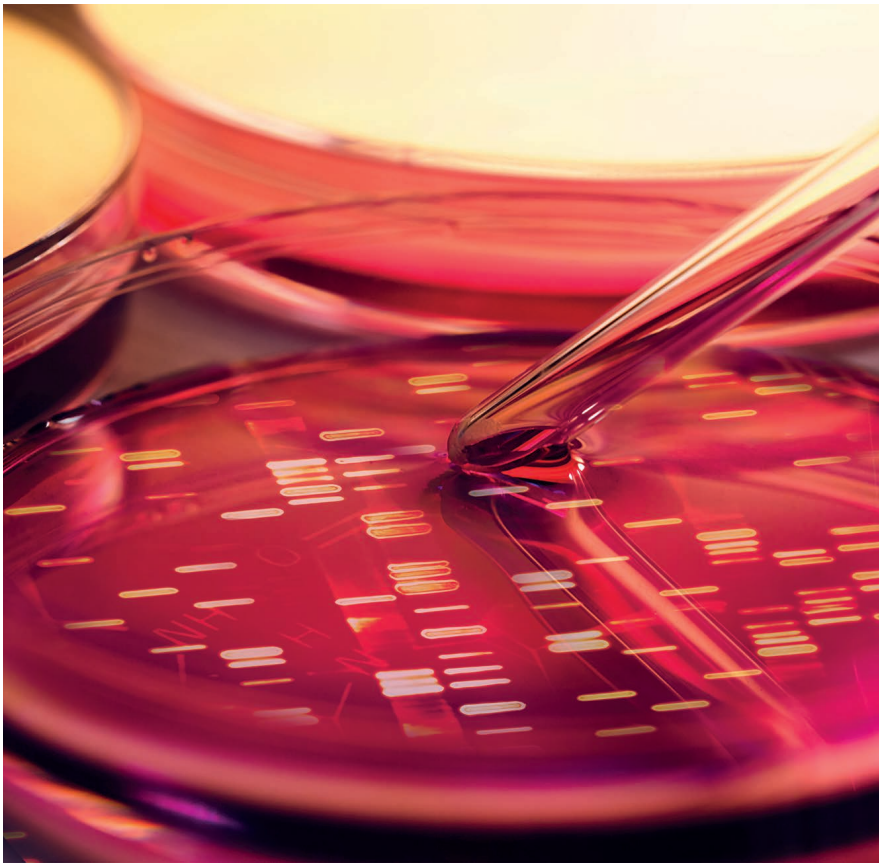
TIA and EIF/SSI funding has supported the CCIA, with **$650,000** being awarded to help purchase an integrated high-content screening system that allows advanced cell-based screening assays and high-content screening of small molecule libraries.

1.3.3
Cell-based therapies

Cell-based therapies are generating a huge amount of interest in the pharmaceutical world, and NCRIS investment in cell therapies has been substantial. Companies investing in such therapies have increased initial public offering statuses and are performing well in the stock markets.

Cell-based therapies rely on large-scale cell manufacturing processes that must meet strict regulatory requirements and compliance, and $500,000 has been allocated for cell-based therapy quality documentation. TIA's THD funding will:

- increase clean room capacity
- subsidise the high costs associated with meeting regulatory requirements for manufacture and regulatory compliance for clinical trials
- implement new technologies including new bioreactor technology
- provide process development laboratories that link basic research with cellular manufacturing facilities.



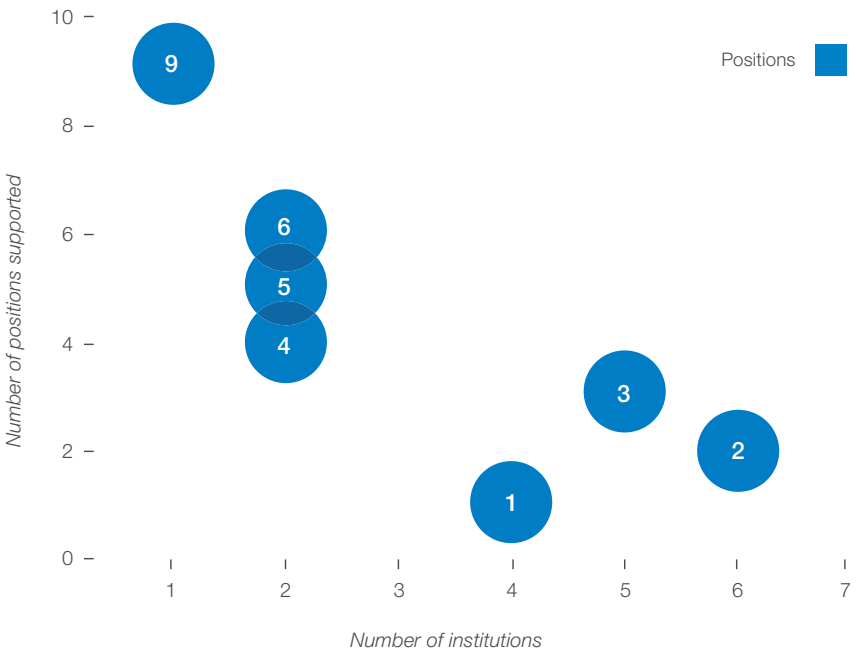
2. Making research investment count

TIA enables access to research infrastructure – hard and soft – so that researchers can see their work come to fruition. Basic research results are tested and translated so that commercial products are realised – increasing the number of Australia's entrepreneurial success stories, improving Australian health care and boosting the Australian economy.

Funding into basic medical research pays off if the results are translated into commercially viable products and devices. For this to happen, multiple factors are needed: access to infrastructure, networks and expert panels; strong collaborations; high-quality researchers and other research staff; and innovative funding opportunities.

TIA precipitates these factors by providing research facility funding. People, sometimes referred to as 'soft' infrastructure, are critical. Having the best equipment is ineffective if the right people are not around to maintain and run it. Unfortunately, staff retention has been a challenge in the past – there are few people with the required skills to perform these jobs. Job security is also an issue, as many positions are supported temporarily by short-term funding. However, TIA is helping to turn this around. Figure 4 shows that 70 staff will be supported by NCRIS 2013 funding in 21 different institutions and networks. This allows Australia to expand its expert skilled workforce.

Figure 4: Support staff positions supported by NCRIS 2013 funding



Note: these positions are not necessarily full-time equivalent.

In the spotlight:

Accessing expert staff essential for upcoming trial to help newborns with bronchopulmonary dysplasia

Dr Rebecca Lim (MIMR) is a principal investigator in an upcoming Phase I clinical trial that will use human amnion epithelial cells to treat bronchopulmonary dysplasia in newborns. To do this, her team will use the Victorian Consortium for Cell-based Therapies (VCCT) Biological Isolator Facility, which was commissioned by St Vincent's Institute (SVI) and Monash Institute for Medical Research (MIMR) and made possible through $2 million of EIF funding.

Being able to access the isolators on a cost-recovery basis will provide huge benefits for the trial, but Dr Lim says 'more importantly, the VCCT provides me with access to experience and know-how of people like Nicole Bleasdale and Tom Loudovaris, who have much more experience with cell manufacturing/processing than an academic researcher like myself. Their experience with Good Manufacturing Practice (GMP) documentation and quality systems, validation of aseptic processing, and even the simple logistics of obtaining and logging quality assurance documents has been an absolute godsend'.

The new BioSpherix Xvivo biological isolators provide a complete barrier from environmental and operator-borne sources of contamination, from start to completion of processing, which is not readily achievable in a standard cleanroom setting.

In the spotlight:
Evolution of a scientific maturity model

The proportion of R&D projects that are commercialised is relatively low. For an institution to boost the turnover of ideas to market, four things are needed: people, processes, tools and data. Organisations are using scientific maturity models to gauge where they are placed in the market in terms of their maturity, or ability, in these four requirements, so they can increase their translational medicine success rates.

TIA is helping organisations move up levels on the maturity model, in particular, with the people, processes and tools component. By helping provide infrastructure, researchers and research institutes can concentrate on what they do best – data generation and interpretation.

2.1
Supporting entrepreneurs and researchers

High-quality researchers and other personnel form the core of successful translational medicine.

This year, TIA is proud to have supported some of Australia's most innovative, high-achieving scientists and clinicians, who have demonstrated genuine entrepreneurial capacity, by providing them with access to expertise.

A $484.2 million Entrepreneur's Infrastructure Programme was announced in the 2014 Australian Federal Budget. The five-year program aims to bring business and research together to commercialise 'good ideas', and will absorb the now-surpassed Commercialisation Australia scheme in 2014–19.

NCRIS 2013 funding is enabling the number of licences, options and patents held by TIA consortia institutions (see Figure 5) – another indicator that researchers and their projects are increasingly moving into the commercialisation arena.

In the spotlight:
Associate Professor Sally-Ann Poulsen, Compounds Australia

Associate Professor Sally-Ann Poulsen's position at Compounds Australia – Chair of the User Committee – allows her to be a part of the discovery of small molecules that can modulate biology and offer better treatment options for patients with disease, something she has been an advocate for doing well since obtaining her PhD in medicinal chemistry.

Compounds Australia (formerly Queensland Compound Library) is a sophisticated compound management facility that securely stores, curates and distributes compound libraries to support the diverse compound management needs of drug discovery researchers. We actively source synthetic compounds, pure natural products and natural product extracts from the Australian chemistry research community. This national compound collection is then made available at low cost to academic and not-for-profit researchers globally. There are no other similar facilities to act as a precedence.

Compounds Australia is full of expert staff who are committed to enabling new collaborations across the chemistry and biology research communities to help seed projects between its members. It is also flexible, in that the molecules are available in multiple formats to suit a variety of research projects.

Assoc Prof Poulsen works with facility manager Moana Simpson to provide solutions that are innovative, and allow the facility to be affordable and accessible, and therefore well used. Compounds Australia's recent collaboration with EU-OPENSCREEN (see Section 3.2.2) will enable even more researcher access to small molecule libraries.

In the spotlight:
Clinical Trials and Biostatistics Unit, QIMR Berghofer Medical Research Institute

Professor Sanjoy Paul – an internationally recognised clinical trialist and biostatistician – heads the Clinical Trials & Biostatistics Unit (CTBU) of QIMR Berghofer Medical Research Institute. Prof Paul and his team play a pivotal role in the development of Australia's translational research capabilities. The CTBU is one of the principal members of the TIA Qld Node, and provides expertise and infrastructure to design, conduct and facilitate high-quality clinical trials, nontrial clinical studies and biostatistical research across many disciplines.

Currently, CTBU is running seven multicentre and multinational clinical trials in different therapeutic areas, as a part of a team of principal investigators. One of the highly acclaimed recently designed studies of Prof Paul is the multinational clinical trial – the SaMpling Antibiotics in Renal Replacement Therapy (SMARRT) study – with Dr Jason Roberts of Royal Brisbane Hospital. SMARRT is a prospective pharmacokinetic study that aims to develop optimised antibiotic dosing guidelines for intensive care unit patients with life-threatening infections.

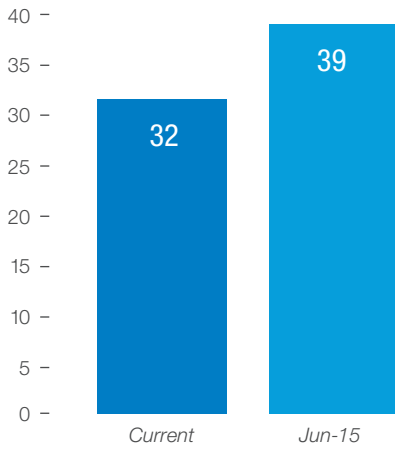
All CTBU professionals are trained in good clinical practice, and all clinical studies are conducted strictly following the international regulatory requirements and pharmaceutical industry standard. Currently, CTBU is conducting clinical studies in collaboration with a number of multinational pharmaceutical companies including Bristol Myer Squib, AstraZeneca and Novo Nordisk A/S.

2.2
Establishing infrastructure and projects

TIA has supported numerous infrastructure and projects this year, some of which are international collaborations, enabling high-quality, outcome-driven research.

Quality accreditation is particularly important to translational research because data that are not reproducible are not valuable. NCRIS 2013 funding has allowed for a 22% projected increase in quality accreditations for the TIA consortia (see Figure 5).

Figure 5: Quality accreditations, current (June 2014) and projected (June 2015)



Cell and Tissue Therapies WA (CTTWA), Royal Perth Hospital

2.2.1
Developing novel clinical trials data management software

TIA, via the EIF, supported the development of a novel clinical trials data management software for the Paediatric Trials Network Australia (PTNA). WebSpirit was launched in July 2013 and is used by 22 trial sites in 18 institutions.

Clinical trials can generate a multitude of data, and good data management is crucial for optimising data analysis. However, data management software like that used by big pharmaceutical companies is expensive and not accessible for investigator-led trials. WebSpirit solved this problem, and provides more efficient communication, multicentre research and reporting on paediatric clinical trial activity conducted under the auspices of the PTNA.

2.2.2
Setting up a world-class cell culture facility

Cell and Tissue Therapies WA (CTTWA) has received nearly $1 million for infrastructure to establish one of the country's top cell culture facilities. The Western Australian Government has co-invested about $250,000, and continues to support the facility via staffing and operations (about $1 million each year).

CTTWA has a strong interest in manufacturing mesenchymal stromal cells (MSCs; see Section 2.3.1). CTTWA have been manufacturing MSCs since 2007 – the only one of its kind in Australia. They now have a licence to manufacture the cells for clinical trials. The cells they produce have shown very good results in trials, pointing to high-quality laboratory procedures. The current challenge is producing the MSCs on a commercial scale, but CTTWA is looking for ways to change this, and continuing infrastructure investments will go towards this goal.

2.2.3
Guiding personalised therapy for leukaemia patients

SA Pathology is collaborating with American-based pharmaceutical companies to improve treatment options for patients with chronic myeloid leukaemia (CML).

The Centre for Cancer Biology (CCB)'s Australian Cancer Research Foundation (ACRF) Cancer Genomics Facility worked with Sequenom in San Diego to develop a novel way to detect mutations in CML patients. Some CML patients have specific mutations that confer resistance very quickly if the wrong drug is given. Unlike standard direct sequencing, the new mass spectrometry technique is sensitive in early detection of these mutations and can lead to personalised medicine for patients.

Ariad Pharmaceuticals, Massachusetts, has developed a drug that overcomes resistance to all single mutations. The new mass spectrometry method developed by CCB was used to examine associations between the detection of low-level mutations and clinical response in patients treated with the Ariad drug in a clinical trial. CCB are now developing next-generation sequencing methods for sensitive mutation analysis, which will allow detection of a broader range of mutations, as well as establish whether mutations are compound or polyclonal. Compound mutations are predicted to influence drug response and lead to resistance, and are therefore important for guiding therapy for patients with identified mutations.

The CCB, an NCRIS recipient in the past, has received more than $400,000 of NCRIS funding from TIA for 2014-15, which will help progress the sequencing methods.

CTTWA, Royal Perth Hospital

2.2.4
Florey Ion Channel Analysis Facility

The Florey Institute Ion Channel Analysis Facility (FICF) fills a crucial gap in Australian translational research – a centralised centre for high-throughput and high-content analysis of ion channels. Ion channels are an important target for many therapies for several orphan and rare diseases, which are often ignored by big pharmaceutical and biotechnology companies.

EIF funding has contributed about $700,000 to the establishment of three core technologies. These allow new research strategies previously not possible in Australia:

- mutation analysis in ion channels
- small molecule drug discovery
- monoclonal antibody targeting ion channels
- ion channel active peptides modulating ion channel function.

2.3 Facilitating clinical trial activity

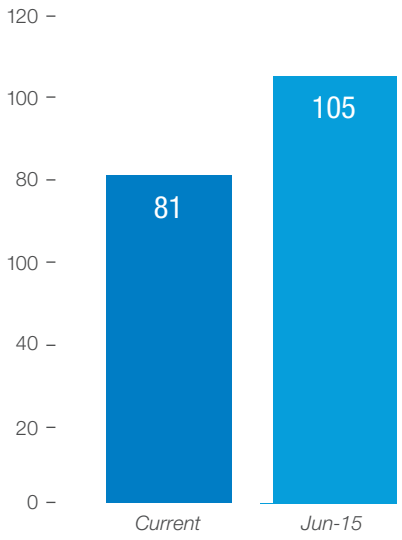
Clinical trials are crucial for translational research, and TIA has supported trials via infrastructure funding. This section highlights some of the returns on investment made to facilities and researchers who have been able to cross the 'valley of death', and progress to Phase I, II and III clinical trials.

Quality accreditation is particularly important to translational research because data that are not reproducible are not valuable.

The ability to provide quality-accredited services not only adds value to the facilities that perform them, but captures more value in the projects they service and the resultant data, leading to better translational outcomes.

NCRIS 2013 funding has resulted in a projected 30% increase in clinical trial activity throughout the TIA consortia for 2014–15 (Figure 6).

Figure 6: Clinical trials within TIA's consortium, current and projected



Note: These figures exclude the 1356 clinical trials currently registered in the ANZCTR.

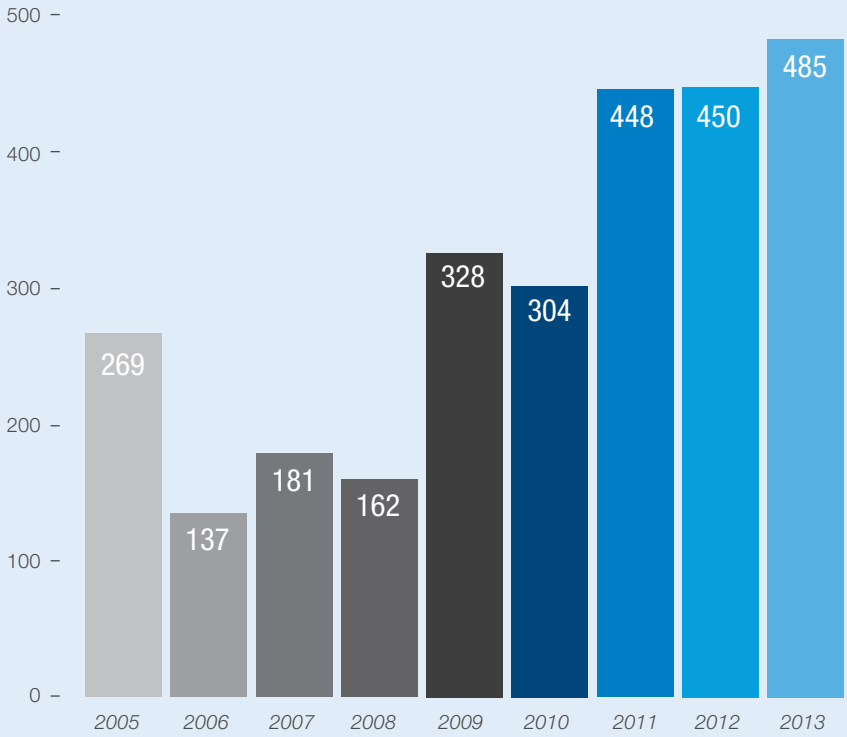
2.3.1 Australian New Zealand Clinical Trials Registry

The Australian New Zealand Clinical Trials Registry (ANZCTR) is a primary registry, capturing clinical trials that take place not just in Australia and New Zealand, but also internationally. It records trials across the full spectrum of therapeutic areas: pharmaceuticals, surgical procedures, preventive measures, lifestyle, devices, treatment and rehabilitation strategies and complementary therapies. The ANZCTR is housed at the University of Sydney's NHMRC Clinical Trials Centre.

Previous EIF/SSI funds saw enhancement of the ANZCTR with a view to increased useability across multiple stakeholder groups. This enhancement provided advanced search functionality to better refine and display online user-initiated searches, as well as providing mechanisms to enable trial data submitted to ethics committees, regulators (such as the TGA) and other specialist registries to be automatically exported and displayed on ANZCTR, reducing duplication of data entry and increasing the completeness of publicly available trial data. It also utilises the now available WHO International Clinical Trials Registry Platform (ICTRP) web service so trials conducted in Australia and / or New Zealand but registered on other registries can be displayed and searched for on the ANZCTR.

Since its creation in 2005, and first receiving EIF/SSI investment in 2011, the ANZCTR has seen notable growth in the number of registered trials (Figure 7).

Figure 7: Open clinical trials registered at the ANZCTR



Clinical trials conducted in Australia and New Zealand, as well as internationally, include substantial numbers of trials conducted by industry, as well as academic trials that are investigator-led (Figure 8).

Primary Sponsor	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014 (up to Oct 2nd)
Charities/Societies/Foundations	21	12	9	12	25	8	22	28	26	14
Commercial sector/Industry	36	20	25	15	33	35	34	31	49	37
Government body	47	21	8	10	19	22	16	26	17	11
Hospital	44	18	33	31	77	58	87	83	97	56
Individual	52	26	59	38	54	78	132	126	113	78
Other	23	6	10	7	8	9	11	16	12	10
Other Collaborative groups	6	0	7	2	12	19	19	12	16	3
University	40	34	30	47	100	75	127	128	155	95
Total:	**269**	**137**	**181**	**162**	**328**	**304**	**448**	**450**	**485**	**304**

Funding Source	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014 (up to Oct 2nd)
Charities/Societies/Foundations	77	44	46	34	66	66	92	106	84	63
Commercial sector/Industry	80	38	53	30	56	58	56	62	86	75
Government body	97	51	66	51	98	92	160	157	126	60
Hospital	23	28	21	20	54	41	87	74	78	43
Other	26	4	7	8	6	9	6	11	6	8
Other Collaborative groups	11	2	5	2	11	14	27	18	18	11
Self funded/Unfunded	25	5	9	24	47	45	58	53	58	40
University	14	24	26	20	47	40	74	78	114	63
Total:	**353**	**196**	**233**	**189**	**385**	**365**	**560**	**559**	**570**	**363**

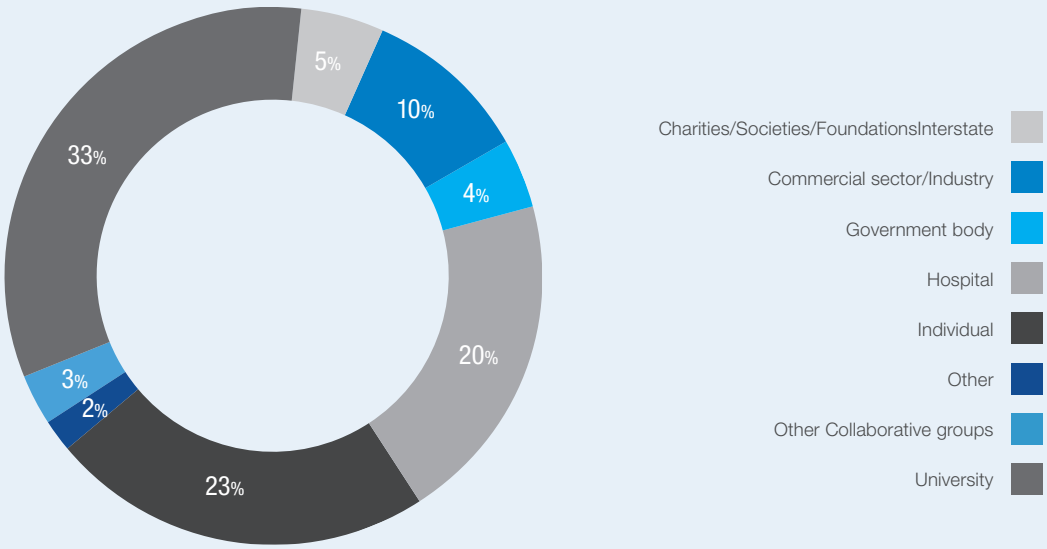


Figure 8: Open industry-based versus investigator-led clinical trials at the ANZCTR for 2013–14

2.3.2
Using immunotherapy to decrease patient infection after transplants

A Phase II study (n = 60) revealed that patients receiving immune cell therapy had a reduced cytomegalovirus (CMV) load and fewer side effects than a control group – positive results that will help launch Phase III studies at Sydney Cell and Gene Therapy (SCGT).

Life-threatening viral infections often affect people who have undergone blood or bone marrow transplants to treat leukaemia and other blood cancers, and are therefore immunocompromised. Hundreds of Australians undergo transplants every year, and reducing the subsequent infection can reduce the burden on patients and the healthcare system. SCGT uses immune cell therapy for three targets: CMV, Epstein-Barr virus and adenovirus.

Immune cell therapy production is complex and requires specialised equipment and knowledge. SCGT has received $3.57 million since 2007 for its immunotherapy-related projects. Since 2009, other projects include pancreatic islet cells for diabetes, immunotherapy for treatment of infections and cancer and gene-modified blood stem cells modified for chemotherapy resistance for children with brain tumours. Total Australian Government funding is more than $9 million to date, including from NCRIS and EIF – administered via TIA.

2.3.3
Helping make mesenchymal stromal cells the next big thing in regenerative medicine

One-third of Crohn's disease patients are unresponsive to conventional therapy, leaving surgery as the last option. This might change after clinical trials at the using MSCs have shown positive results.

TIA funding provided the opportunity for the Phase I trials, in collaboration with the United States–based Broad Medical Research Program. The trials were a partnership between several Australian medical institutes, but were hosted at the facilities at Cell and Tissue Therapies WA (CTTWA), and the Department of Gastroenterology at the Royal Perth Hospital.

Twelve out of the 15 patients who received conventional plus MSC treatment showed improvements in symptoms of Crohn's disease, and eight showed remission. This sets the stage for Phase II studies.

MSCs were originally trialled in graft versus host disease (GVHD) patients. Both diseases are autoimmune and result in chronic inflammation. After promising results in GVHD trials, researchers realised the MSCs may be important in controlling Crohn's.

The results are groundbreaking, due to the inherent properties of MSCs (they are a universal donor cell, meaning the cells do not need to be typed) and the increasing numbers of autoimmune diseases.

MSCs have a promising future in regenerative medicine therapies. MSCs have been studied for use in diabetes and multiple sclerosis, in addition to GVHD.

2.3.4
Giving Madeleine Pharmaceuticals a hand

The Australian Centre for Pharmacometrics (ACP) has been essential for helping Madeleine Pharmaceuticals develop their cardiac peptide to help treat heart failure. This success story provides a perfect example of industry engagement.

Madeleine Pharmaceuticals, a small-to-medium enterprise, wanted to target a particular steady-state plasma concentration that was integral to the protocol of a trial. ACP created a population pharmacokinetic model of subject data and suggested possible dosing for the next phase of study. This approach allowed Madeleine Pharmaceuticals to design a dosing regimen for investigation in their trial protocol to ensure a meaningful and cost-effective trial outcome was achieved.

About 30,000 Australians are diagnosed with heart failure every year and recurrent hospitalisations cost the Australian healthcare system more than $1 billion each year. Heart failure management relies on lifestyle changes and pharmacotherapy. Madeleine Pharmaceuticals wanted to establish parameters for its congestive heart failure drug in a way that would help minimise the associated costs of clinical trials that are required to ensure drug safety and efficacy – helping Australia to be at the forefront of 'smart drug development' that will reduce drug developments costs and therefore increase investment returns.

The ACP has received $600,000 funding through TIA and EIF/SSI to purchase computers and associated software used for pharmacometric modelling and analysis.

MADELEINE
Pharmaceuticals Pty Ltd

3. Collaborating with key players

TIA is proud to be a part of developing the world's first national supply chain for translational research. Although similar networks exist in clusters elsewhere, none are on the national scale that Australia can boast. Furthermore, this supply chain is being extended overseas.

In 2012, TIA mapped all of the capabilities forming Australia's translational research network. Now that these core institutions are identified, TIA is working to feed collaborations and diminish gaps to construct a national supply chain. This chain provides a crucial resource – all infrastructure is identified and researchers are easily able to determine where to go to get their project off the ground. TIA's role includes enabling researcher access to facilities.

Access to international expertise and facilities is also crucial to product commercialisation. TIA has signed multiple memorandums of understanding (MoUs) with important European Union (EU) networks that will increase Australian researcher success rates.

3.1 Maintaining and extending the national supply chain

In 2011–12, we identified and mapped the capabilities across Australia (see Figure 9). This map will be used to develop and expand the national network, based on the Qld Node.

As a step towards nationalising TIA's Queensland Node, TIA intends to establish the Australian Therapeutic Pipeline (ATP), to provide a pathway for researchers trying to develop a new biopharmaceutical or drug. The ATP will comprise facilities and service providers – including Phase I and II clinical trial centres – whose capabilities have been identified as critical to therapeutic product development.

Mapping the supply chain not only provides information to researchers who want to access drug development services, but also helps service providers better understand their place in the supply chain and to strengthen relationships between service providers who are at earlier or later stages of development.

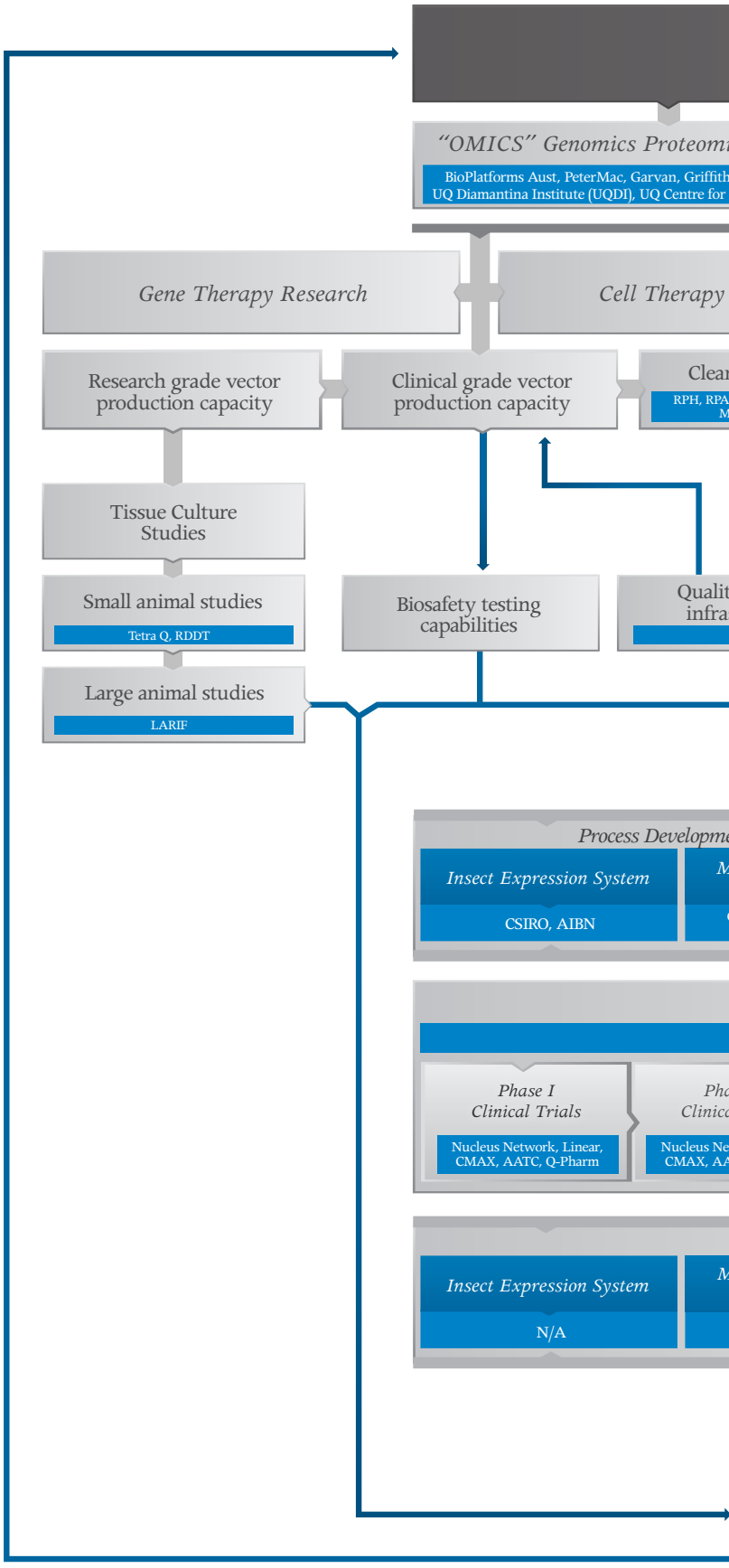
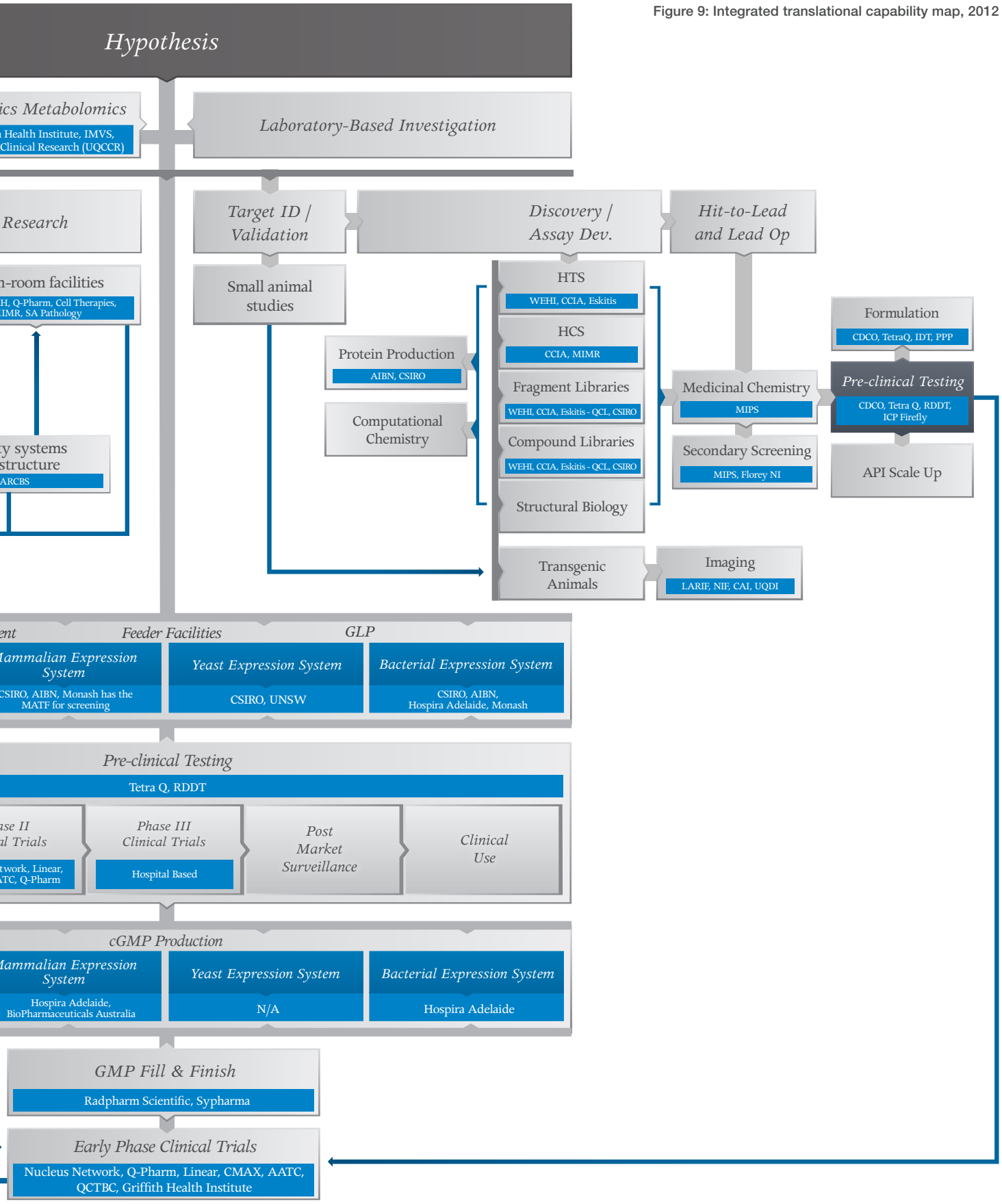


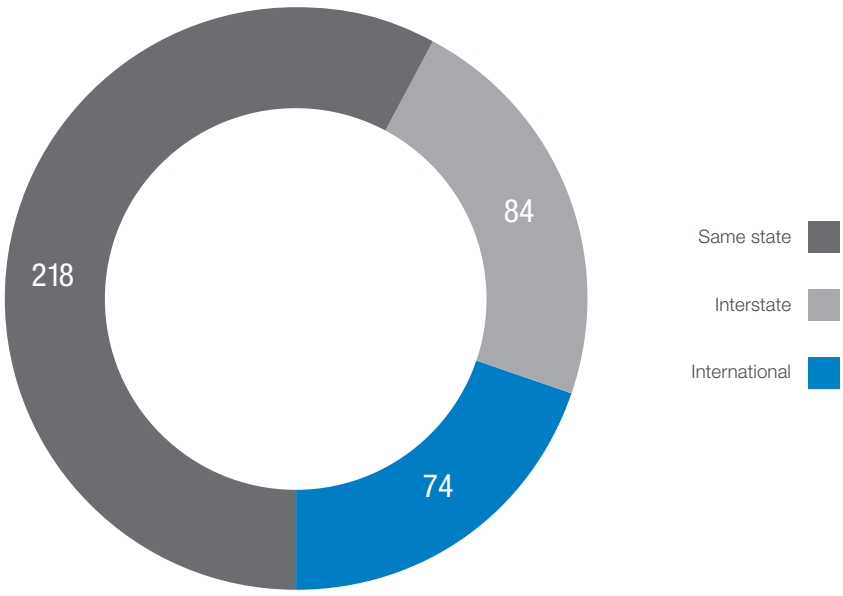
Figure 9: Integrated translational capability map, 2012



NCRIS 2013 funding will also be used to increase researcher access to facilities across the Australian supply chain – external use as shown in Figure 10. Notably, this represents a projected 12% increase in internal access (data not shown) and a 54% increase in external access – including a 64% increase in international researcher access (data not shown). Facility infrastructure utilisation rates are also expected to increase, from 57% in 2013–14 to 73% in 2014–15.

The Australian Government Department of Education's NCRIS 2013 funding will enable a projected 12% increase in internal access and a 54% increase in external access – including a 64% increase in international researcher access to facilities.

Figure 10: External researcher facility access to TIA's consortium in 2013–14



Notes: Data only available for all institutions that received NCRIS 2013 funding.

3.2 Creating an international supply chain

Although Australia provides a substantial amount of infrastructure and resources to its researchers, all research benefits from international collaborations. This allows access to a wider pool of resources, including expertise, equipment and facilities, and networks.

3.2.1 Making our mark at international conferences

Pharmaceutical Sciences World Congress

TIA had a strong presence at the 5th International Pharmaceutical Federation (FIP) Pharmaceutical Sciences World Conference (PWSC). The 2013 PWSC – themed 'Pharmaceutical sciences beyond 2020: the rise of a new era in health care' – provided an opportunity for Australia to promote itself as a leader in pharmaceutical development. In turn, the conference allowed the TIA representative, CEO Dr Stewart Hay, the chance to exchange ideas with about the latest research and development opportunities.

FIP comprises pharmacists and pharmaceutical scientists from around the world. On the first day, TIA hosted a workshop, 'Therapeutic development in Australia', which was targeted to national and international researchers. The audience was given response devices to help focus the discussion on topics of highest priority. This unique approach allowed TIA to compile important data on the needs of pharmaceutical scientists, and their understanding of available services and assistance in translational medicine.

Healthy Ageing Theme conference

Connecting with the world's best continued at two events hosted by the Australian Government Department of Education in 2013. The meetings advanced collaboration between Europe and Australia in research infrastructure, including infrastructure to exploit large and complex research datasets. Several actions healthy ageing–specific actions were agreed to. TIA and the Population Health Research Network will help conduct a review of currently available Australian and European online learning tools and content with the goal of sharing the best examples (led by the National

Imaging Facility [NIF] and Euro BioImaging).

These ideas were furthered at a conference in May 2014, which brought together some key networks from Australia and the EU to expand on some capabilities. The conference served as a reminder that the same hurdlers are faced by researchers here and in Europe. These hurdles can, in part, be solved together, including:

- developing a position paper on career pathways
- sharing knowledge and experience about engagement with our users to maximise benefits
- reviewing currently available e-research tools, and developing clear guidelines and policies for managing large amounts of data
- developing standard operating procedures to provide confidence to the users of multisite research facilities
- identifying themes and authors for online training modules, for both facilities and users.

3.2.2 Signing memorandums of understanding with leading European centres

TIA is committed to providing open access to databases, libraries and other repositories for researchers. The following MoUs will provide researchers expanded access to libraries in Australia and Europe.

TIA and Compounds Australia collaborate with EU-OPENSCREEN

TIA, Compounds Australia and EU-OPENSCREEN signed an MoU that will see a new Australia – EU collaboration.

The MoU will enable Australian researcher access to potential substrates for new pharmaceuticals from Europe. European researchers will also be able to access screening libraries in Australia.

EU-OPENSCREEN is a network of European compound libraries and screening centres focused on drug discovery, and Compounds Australia is the national compound collection at Griffith University's Eskitis Institute.

> ***This [MoU] brings us a big step forward in joining forces with other continents to advance our understanding of how chemicals affect molecular mechanisms of complex biological processes.***
>
> – Dr Ronald Frank, Leibniz-Institut für Molekulare Pharmakologie, EU-OPENSCREEN Coordinator

TIA and ECRIN

The European Clinical Research Infrastructure Network (ECRIN) is a not-for-profit infrastructure organisation targeted towards clinical trials. TIA and ECRIN have signed an MoU earlier in 2014 that will enable collaborations between Europe and Australia in clinical trials research.

TIA and EATRIS

The European Advanced Translational Research Infrastructure in Medicine (EATRIS) has signed an MoU with TIA, enabling a multinational network to address systemic issues with translational health research.

EATRIS and TIA will investigate opportunities to share information about the European and Australian therapeutic product development pathways. Both parties will share information relating to systemic improvements to quality compliance among participating facilities and TIA will perform this partly by hosting the International Regulatory Repository.

Ms Ana Arana Antelo, Head of Unit, Research Infrastructures, DG Research and Innovation, European Commission; Professor Ronald Quinn, Director, Eskitis Institute for Cell and Molecular Therapies; Dr Stewart Hay, CEO, Therapeutic Innovation Australia; Ambassador Duncan Lewis; Dr Ronald Frank, Leibniz-Institut für Molekulare Pharmakologie, EU-OPENSCREEN Coordinator

4. Governance and structure

4.1 Board

TIA's five Board members are highly accomplished individuals with valuable knowledge in both public and private sectors.

Mr Terry Slater

BSc, BEc, MPH, FAIM

Chairman

Mr. Slater was the CEO of Australians Donate, the peak body of the organ and tissue transplant organisations in Australia. Terry was CEO of the Therapeutic Goods Administration (TGA) for nine years and has subsequently been a consultant for many organisations in health services and semigovernment bodies.

Dr George Morstyn

MB BS B Med Sci PhD FRACP MAICD

Co-chair TIA NCRIS Expert Advisory Committee

Dr Morstyn is applying his experience in translational medicine in the academic commercial interface. He is on the boards of Proacta (based in Auckland and San Diego developing cancer therapy), Chemgenex, AMT (gene therapy), and Neuprotect. Dr Morstyn is Deputy Chairman of the $1 Billion Parkville Comprehensive Cancer Centre, he is a Director and Chairman of the scientific advisory Board of Symbio (Japan based biotech developing drugs for cancer treatment) and Chairman of GBS Ventures. Dr Morstyn also advises The Walter and Eliza Hall Institute on commercialisation.

His interest in translational research dates back to 1979 when he commenced a PhD with Professor Don Metcalf. Dr Morstyn became head of the Clinical Program of the Ludwig Institute for Cancer Research in Melbourne. He was principal investigator of the earliest studies of G-CSF, GM-CSF and IL-4. Dr Morstyn joined Amgen in 1991 as an adviser, later became Vice President of Medical and Clinical Affairs, then Chief Medical Officer and in 1999 Senior Vice President of Development.

Mr Rob Anderson

FCA, FAICD

Company Secretary, Chair of the Audit Committee

Mr. Anderson is currently the MD of Orthogen which operates in the field of cell therapies and is principal of Anderson Business Consultants. Rob has significant experience consulting to government and industry. He has extensive commercial and financial experience in a diverse range of industries and business structures including as Partner (Audit and Advisory) Deloitte Touche Tohmatsu.

TIA would not be successful without some key players, including our governance Board and expert advisory committees.

Ms Elizabeth Furler

BA (Social Work)

Member of the Public Health Association of Australia

Ms Furler was a senior health executive in the Commonwealth and several state health authorities. She also served as the CEO of the Royal Australian College of General Practitioners, the Principals Australia Institute and TRACsa, as General Manager with the Australian National Training Authority and Executive Director with the Department of Education and Children's Services in South Australia. She is currently a consultant for organisations in health, early childhood development and education.

Professor Judith Whitworth AC

MBBS MD PhD DSc (Melb) MD (Hon, Sydney) MD (Hon, UNSW) DSc (Hon, Glasgow) DLett (Hon, Charlers Darwin) LLD (Hon, Melb) FTSE FRACP FAICD

Co-chair TIA NCRIS Expert Advisory Committee, Chair Clinical Trial Infrastructure Committee

Professor Whitworth is an Emeritus Professor at the Australian National University where she was previously Director of the John Curtin Schools of Medical Research. She is a Fellow of the Australian Academy of Technological Sciences and Engineering, the Royal Australasian College of Physicians, and the Australian Institute of Company Directors. Professor Whitworth has chaired the Medical Research Committee of the NHMRC and is a Past-President of the Australian Society for Medical Research, and the High Blood Pressure Research Council of Australia as well as an Honorary Life Member of the Australian and New Zealand Society of Nephrology.

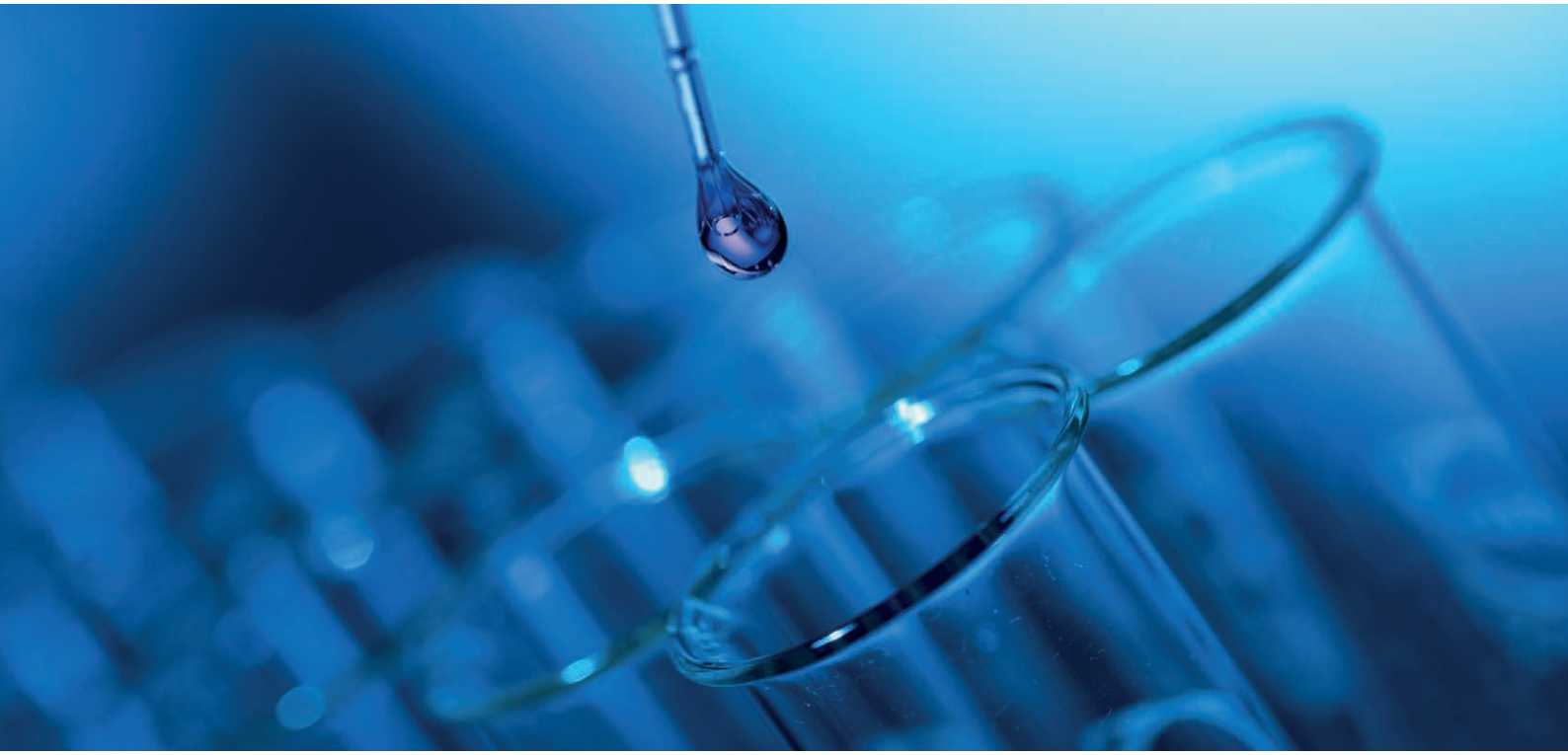
Previous appointments include Commonwealth Chief Medical Officer of Australia, Chair of the World Health Organization Global Advisory Committee on Health Research, and Professor of Medicine at St George Hospital, UNSW. Professor Whitworth was made a Companion in the Order of Australia in 2001, for service to the advancement of academic medicine and as a major contributor to research policy and medical research administration in Australia and internationally, and was also a recipient of the Centenary Medal. She was Telstra ACT Business Woman of the Year 2002 and in 2004 was ACT Australian of the Year. Other awards include the Curtin Medal, the Kincaid Smith Medal, the Florey Medal and the RACP Medal.

4.2 Committees

TIA's expert advisory committees provide invaluable advice in numerous research areas, including translational medicine, pharmaceutical and other therapy development, and capability pathways:

- NCRIS 2013 Expert Advisory Committee
- Virtual Pharma Committee
- Queensland Node Strategic and Executive Committees
- Clinical Trials Infrastructure Committee
- Biopharmaceutical, Biomaterial and Medical Device Committee
- Cell and Gene Therapy Committee.

The Virtual Pharma Committee is expected to play an important role in the future. When it becomes fully operational, public-sector researchers will have access to their free development advisory service.



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