Australian Health Genetics/ Genomics Survey 2017 Report of Key Findings to: Department of Health

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RCPA
The Royal College of Pathologists of Australasia

This report has been prepared on behalf of the Royal College of Pathologists of Australasia, for the Department of Health. The views expressed in this document do not necessarily represent the views of either organisation. This report is based on data provided by participating laboratories.

Contents

1. Executive Summary

Genetics and genomics is a rapidly developing field in medical science. The National Health Genomics Policy Framework (the Framework),[1] endorsed by the Council of Australian Governments Health Council in November 2017, has been established to better integrate genetics and genomics into the Australian health system. The Framework identifies five key priority areas for action: patient-centred approach, workforce, safety and quality of services, sustainable financing, and data. To support its implementation, the Australian Health Ministers' Advisory Council (AHMAC) commissioned a national genetic and genomic testing and activity stocktake (the Stocktake).

Previous surveys of genetic testing in Australia were performed by the Royal College of Pathologists of Australasia (RCPA) in 2006 and 2011. The aims of the Australian Health Genetics/ Genomics Survey 2017 were to provide updated information on the nature, availability and volume of genetic/ genomic tests arranged for Australian patients, to make comparisons with historical data, to provide information about workforce change requirements and to facilitate modelling for future service provision.

All Australian laboratories known to have offered genetic/ genomic tests that yielded results with medical utility during the 2016 to 2017 financial year (1 July 2016 to 30 June 2017), irrespective of accreditation status, were invited to participate (87 laboratories).

The overall participation rate was 95.4% with four laboratories not responding. Key findings of the survey are presented in Box 1 (Survey Summary).

While participation levels were high, data submissions from some laboratories were incomplete. Among the responding laboratories, 6 laboratories (7%) did not provide information about tests completed and 8 (9.5%) did not provide details about accreditation status, clinical referrers, staffing and supporting infrastructure.

Feedback offered from laboratories revealed that most still do not have the capability to readily extract much of the data required by the survey. Although this issue had been raised and discussed in the 2006 and 2011 reports, many laboratory managers explained that laboratories still had only limited capability to extract and summarise the data being sought by these surveys. Many managers explained that although most laboratory information systems can be set up to capture prospectively these data, a substantial investment would be required to establish these processes. The ongoing absence of an organised system to capture prospectively agreed key performance indicators of genetic/ genomic testing across Australia threatens the feasibility of future surveys, particularly with the ongoing growth within the sector.

Another risk for future potential surveys is the reluctance of some private laboratories to participate due mainly to concerns about commercially sensitive information.

It is apparent that solutions to these issues must be identified and implemented to retain the possibility of conducting future surveys.

1. National Health Genomics Policy Framework 2018 – 2021. ISBN: 978-1-76007-327-5; Online ISBN: 978-1-76007-328-2

Box 1: Survey Summary

Number and type of laboratories

Eighty-seven Australian laboratories delivered various categories of genetic testing, including biochemical genetics, newborn bloodspot screening, pregnancy-related or population screening tests during the 2016 to 2017 financial year (1 July 2016 to 30 June 2017). All were invited to participate in the Stocktake. Eighty-three of 87 laboratories (95.4%) submitted full or partial returns.

Eighty of these laboratories provided details about their NPAAC category, accreditation status and test numbers. Of these, 51.3%, were in the public sector and delivered 45.1% of all completed tests; 30% were in the private sector delivering 53.6% of all completed tests; 15% were research delivering 0.2% of all completed tests, and 3.8% were Catholic/ schedule 3 delivering 1.1% of all completed tests.

Laboratory accreditation

Seventy-two of 80 laboratories (90%) were NATA accredited. Non-accredited laboratories performed 0.14% of all tests. Compared with 39 participating NATA accredited laboratories in 2011, the number of accredited laboratories has risen by 85% over 5 ½ years. Thirty-two of the 72 laboratories offering genetic/ genomic testing were also accredited for massively parallel sequencing, of which twenty-two (69%) were accredited under the 2017 NPAAC requirements.

Number of tests

A total of 1,181,923 tests were reported. They comprised 660,150 genetic/ genomic tests (constitutional – 545,029; cancer – 115,121); maternal serum screening (146,719); newborn bloodspot screening (307,770), and biochemical genetic diagnostic tests (67,284).

Genetic/ genomic tests in 2011 were grouped as molecular or cytogenetic. Using these categories, the volume of molecular genetic tests has increased by 73% over the past 5 ½ years. By contrast, the volume of cytogenetic tests fell by 40%.

Referral sources and test indications

The most common referral sources for genetic/ genomic tests in 2016/17 were General Practitioners (27.7%), Obstetricians/ Fertility/ Fetal Medicine Specialists (21.1%) and Pathologists (15.4%). Other significant clinical referral sources were Paediatricians (8.1%), Clinical Geneticists (6.6%) and Oncologists (5.4%).

The most common reasons for testing were for diagnostic purposes for constitutional genetic conditions (55% of requests) or for cancer (12%). Other clinical indications included various forms of “cascade testing” of relatives for familial variant(s); therapy selection; minimal residual disease (leukaemia) and transplant monitoring; population screening; several categories of prenatal testing, and preimplantation genetic screening.

Test categories

In the constitutional setting, targeted analysis to assess for the presence or absence of a predefined genomic variant(s) represented the largest test category (78.3%). This category also accounted for most cancer tests (71.1%), although FISH/ ISH analysis represented a higher proportion of cancer-related targeted tests (20.2%) than constitutional targeted tests (1.2%). Chromosomal karyotyping represented 17.5% of cancer-related and 10.2% of constitutional tests. By contrast, chromosomal microarray analysis accounted for 7.0% of constitutional and 1.3% of cancer tests. The other listed test categories were sequencing-based: grouped as single gene; 2-49 genes; 50+ genes; exome, and genome, as well as gene expression studies.

Workforce
The total number of FTEs identified by this survey was 1287.8. This represents a 27% increase in workforce compared with 2011; however, account should be taken of the wider scope and the inclusion of non-accredited laboratories in the 2016/17 Stocktake.

Laboratory supervision
Sixty-one of 81 laboratories (75.3%) included staff with locally-recognised professional qualifications indicating scopes of practice in genetics (FRCPA Genetics, FFSc Genetics, FHGSA, recognised overseas qualifications or a combination).

Thirty-three laboratories (40.7%) included a supervising Genetic Pathologist. Seventeen (21.0%) did not have access to any supervising Pathologists (FRCPA, any discipline). Forty-nine (60.5%) had a supervising scientist with FFSc (genetics) or FHGSA. Nine laboratories (11.1%) did not have access to either a Pathologist (FRCPA, any discipline) or scientific staff with any locally-recognised professional qualification indicating proficiency in genetic laboratory practice.

An assessment was also made of the numbers, and associated percentages, of tests performed in the absence of medical or scientific staff with professional qualifications relevant to genetic laboratory practice (FRCPA Genetics, FFSc Genetics or FHGSA). These included targeted testing directed towards predefined variants – approximately 52,200 tests (10.5%); targeted testing for undefined variants (1 to 49 genes) – 10,600 tests (36.4%); targeted testing for undefined variants (≥ 50 genes) – nil (0%); untargeted testing by karyotype – 3,200 (4.2%); untargeted higher-resolution testing by microarray – 4,600 (11.6%), and whole exome or genome sequencing – 300 (44.7%).

Interstate and international transfer of samples for testing
The volume of samples transferred interstate or overseas for genetic/ genomic testing continues to rise. The percentage of interstate transfers has more than doubled over the past 5 ½ years, from 9.6% in 2011 to at least 19.8% in 2016/17. For constitutional, cancer and biochemical genetic tests, the percentages of interstate transfers were 23%, 12% and 10%, respectively.

As many laboratories did not provide information on the state/ territory-of-origin of tested samples, the overall rate of increase is likely even greater.

The reported number of samples transferred to international laboratories has also risen – from 2,766 in 2011 to 3,625 in 2016/17 (a 31% increase). As described in the report, numerous additional samples are known to have bypassed the laboratories contributing to the Stocktake, which means that this number is an underestimate.

Laboratory informatic infrastructure
Laboratories used a variety of systems for sample registration, tracking and report storage. Most used Laboratory Information Management Systems (LIMS), local electronic records/ databases located on either laboratory/ hospital servers, or local hard drives. Fewer than 10% of laboratories, both service and research, used laboratory workbooks or stored reports as hardcopies.

Genomic informatic infrastructure
Genomic data generated from patient samples were stored on a variety of platforms, of which hospital servers (29%), local laboratory servers (21%), and “multiple storage systems” (22%) were the commonest options. Approximately a third of service laboratories considered their data storage facilities to be suboptimal; in particular, laboratories indicated that details of locally-identified variants were not retained in a searchable local database for future reference.

International genetic/ genomic databases

Approximately three-quarters of laboratories did not contribute details of locally identified genomic variants to international variant databases.

Reporting (turnaround) times

Substantial improvements were observed in the median reporting times for targeted molecular assays since 2011, however the range of reporting times was broad and a substantial proportion of results were delivered beyond published recommended turnaround times. Median reporting times for molecular tests involving screening genes for unknown disease-causing mutations have lengthened since 2011. The 2016/17 median cytogenetic reporting times were unchanged from 2011; however, the 90th centile reporting times for constitutional- and cancer-related chromosomal karyotyping both exceeded the current recommended standard for Australian laboratories.

Funding

The 2016/17 survey data revealed that funding arrangements for genetic tests have changed substantially. For within-state tests, federal funding (Medicare) covered almost half (49%) of within-state tests in 2016/17, compared with 35% in 2011. There have been corresponding falls in the proportion of tests funded by most other sources. Federal funding covered approximately two thirds of tests performed on interstate samples in 2016/17. Most of the remaining interstate tests were funded directly by patients. On the background of an increasing number of tests being transferred across state borders, the overall proportion of interstate tests paid for by patients has doubled to approximately one quarter of tests.

2. Definitions and Terminology

Survey instrument(s): Spreadsheet(s) used to collect data for the survey and the accompanying cover letter, guide for participants, and confidentiality agreement (see Appendix B).

Genetic: Genetic testing seeks to identify changes in chromosomes, genes, or proteins. Identified genetic changes (variants) may confirm the diagnosis of a suspected disorder, predict the likelihood of developing or passing on a genetic condition, or predict response to medication. Several methods can be used for genetic testing:

- **Gene tests** (or molecular tests): study short lengths of DNA, a single gene, or multiple genes to identify variations or mutations that lead to a genetic disorder.
- **Chromosomal tests**: analyse whole chromosomes or long lengths of DNA to assess for large genomic changes, such as an extra copy of a chromosome, causative of a genetic condition.
- **Biochemical tests**: study the amount or activity level of proteins; abnormalities in either can indicate changes in genes that result in a genetic disorder.

Genomic tests: The study of multiple genes, which may include analysis of all genes across the human genome, involves the use of massively parallel sequencing technology and microarray technology.

The term **genomic testing** is increasingly used to describe this type of testing. It is noted that the term, which is a concatenation of “gene” and “chromosome”, is increasingly used as a synonym for genetic testing. Notwithstanding this trend, the term “genetic” is used in this report to refer to testing for pre-defined variants or sequence- /copy number-based screening of a limited number of genes, while “genomics” is used for massively parallel sequencing-based screening of many genes – up to the level of whole exomes and genomes.

Within this survey, a **single test** is defined according to the clinical referral. For example, a request for simultaneous sequence analysis of fifty genes (a 50-gene panel) associated with cardiac disease is counted as a single test.

Constitutional test: Refers to testing for a genetic variant (alteration) that is present in every cell of the body and which may also be inherited.

Cancer (somatic) test: Refers to testing for an acquired, non-heritable, genetic variant in the context of cancer.

Test requests: Laboratory investigations requested by clinical referrers.

Test target/ scope: The genomic location or region interrogated by the test, comprising subcategories of: A. targeted testing of specified genetic variants; B. testing for undefined variants in specified genes, or C. untargeted testing.

A. ***Targeted testing for presence/ absence of specified genomic variation*** includes clinically-specified analysis for the following:
- a single variant (small nucleotide level)
- multiple targeted variants in a single gene (small nucleotide level)

- multiple targeted variants in multiple genes (small nucleotide level)
- targeted genome deletion(s)/ duplication(s)/ dosage analysis
- targeted genome rearrangement analysis
- gene amplification analysis
- genome mutability analysis
- targeted methylation analysis

B. ***Testing for undefined variants in specified genes*** involves targeted analysis of the genomic sequences of one or many genes, all of which are associated with specified clinical phenotypes. Typical clinical applications include targeted "gene panel" testing for constitutional disorders (e.g. inherited muscle diseases) or specified cancer presentations (e.g. melanoma).

C. ***Untargeted testing for known and unknown variants across the genome*** may be performed by "exome" or "genome" sequencing. Conceptually, untargeted genome-level testing also includes lower resolution analysis by chromosomal karyotyping or DNA microarray analysis.

Biochemical genetic tests: The scope of testing includes diagnostic testing for inborn errors of metabolism, newborn bloodspot screening and prenatal biochemical marker screening for the common chromosomal aneuploidies.

Test method

Laboratories were asked to provide details of the analytical approach(es) deployed to interrogate the genomic location(s) required for each test request.

Examples of test methods include microscopy-based karyotyping of banded chromosomes and fluorescent in-situ hybridisation (FISH); numerous different nucleic acid amplification-dependent/ readout assays which utilise a range of detection methods such as testing for the presence or absence of a restriction enzyme cutting site; differential oligonucleotide hybridisation; single nucleotide primer extension (minisequencing); Sanger sequencing, and massively parallel sequencing.

Clinical referral category

The clinical reason for performing a test, including:

Diagnostic assessment/ family cascade testing: Refers to testing of an affected patient (of any age) to determine the genetic basis for their symptoms or presentation. For the purposes of this survey, this category also included testing of asymptomatic individuals (prenatal not included) who, on the basis of family history, were known to be at high risk of carrying a known familial variant. It also included diagnostic testing on post mortem specimens.

Subcategories

- Constitutional - symptomatic index cases patient
- Cancer – tumour/ blood/ bone marrow samples
- Family segregation analysis (to assist variant classification)

- Familial cascade testing of a known disease-causing variant (including presymptomatic/ predictive; excluding carrier testing for recessive/ X-linked disorders)
- Recessive/ X-linked carrier testing (high prior risk)

Therapy selection/ monitoring: Testing that directs therapeutic/ prescribing decisions; or monitoring allogeneic transplant tissue, or for evidence of tumour recurrence.

Subcategories

- Minimal residual disease/ transplant monitoring
- Tumour sample genotyping to guide therapy selection
- Pharmacogenomic testing (constitutional) to guide therapy selection or drug dosage

Pleiotropy: The genetic effect of a single gene on multiple phenotypic traits, including the occurrence of different clinical phenotypes arising from differing genomic variants positioned across the gene.

Prenatal: Diagnostic testing on fetal tissue (amniocentesis, chorionic villi, blood and other tissue), or screening of fetal DNA in maternal blood.

Pre-implantation genetic testing: Testing an embryo (prior to implantation), either because the embryo is at high risk of having inherited a monogenic disease or to screen for chromosomal aneuploidy.

Population screening: Testing of a healthy person without a history to suggest a health hazard above the background population risk.

Subcategories

- Newborn Bloodspot Screening
- Genetic disease detection (population risk)
- Recessive mutation carrier screening (population risk)

Reporting (turnaround) time: Time taken for testing to be performed, measured in calendar days from receipt of the sample within the testing laboratory.

State-of-origin of test request: The originating source of each test request (i.e. the state-/ territory-of-origin of the sample).

Interstate samples: Samples transferred across Australian state/ territory boundaries.

International samples: Samples either transferred to or received from overseas centres.

Funding source for State samples: The source of funding for intrastate sample tests, selected from:

- **Federal:** refers to any form of Federal Government funding, including Medicare and Veteran's Affairs.
- **State:** refers to State Government funding, irrespective of recharge arrangements between health units.

- **Grants/ Contracts:** refers to research or commercial funding.
- **Patient**: refers to testing paid for by patients and their families.

Funding source for Interstate samples: The source of funding for Interstate sample tests, selected from:

- **Federal, Grants/ Contracts** or **Patient**: defined as above.
- **Referring service:** refers to charges billed to the referring service (laboratory or clinical service).
- **No charge:** refers to tests completed with no associated cost recovery.

3. Introduction

3.1 Background to Project

Genetic and genomic testing is a rapidly developing field in medical science. To ensure that the Australian public gains access to the numerous health care benefits emerging from clinical applications of genetics/ genomics across all pathology services, the Commonwealth Government requires up-to-date details about the current range and volume of tests being provided.

- On 18 March 2016, the Australian Health Ministers' Advisory Council (AHMAC) agreed that the Commonwealth would lead a project, in consultation with jurisdictions, to develop a national whole-of-governments system-focussed policy framework for genetics and genomics, reporting to AHMAC.
- The development of the National Health Genomics Policy Framework 2018-2021 (the Framework) was led by the Commonwealth, with input from a time-limited jurisdictional advisory group with representatives from all states and territories (the National Health Genomics Policy Framework Advisory Group). The Framework was finalised by Health Ministers in late 2017.
- Developing a whole-of-governments and system-focused Framework, with a person-centred approach to outcomes, is necessary to ensure consistency of action across Australia. The Framework will support better coordination across the health system to ensure the potential benefits of genetics and genomics are harnessed in an efficient, effective, ethical and equitable way. Crucial to this is ensuring system preparedness and community readiness for this disruptive technology.
- The Framework, which has been informed through extensive stakeholder consultation during 2016/17, identified five key priority areas for action: patient-centred approach; workforce; finances; services, and data.

As a first step to support implementation of the Framework, AHMAC commissioned a national genetic and genomic testing and activity stocktake (the Stocktake). The purpose of the Stocktake was to provide a summary overview of genetic/ genomic testing services provided over a recent 12 month period to Australian patients for disease diagnosis, monitoring, treatment, disease prevention, prediction or predisposition assessment.

- There was an expectation that the Stocktake would establish a new national baseline for genetic/ genomic testing and associated activities:
  - to inform the development of an Implementation Plan, which would outline priority activities for implementation, funding and resource implications, and the roles and responsibilities of governments and other stakeholders; and
  - to support ongoing monitoring, reporting and evaluation of the Framework.
- The Stocktake, together with the outcomes of a comprehensive gap analysis, needs assessment and stakeholder consultation, was expected to inform further advice to governments to address current and emerging priorities, as resources permit.
- The governance arrangements for implementation and funding would be a matter for COAG Health Ministers.
- In May 2017, the Commonwealth engaged the Royal College of Pathologists of Australasia (the RCPA) to undertake the preliminary scoping work to support the national genetic/ genomic testing stocktake.

- While the RCPA led similar projects in 2006 and 2011, this stocktake captures more information about the range of tests being delivered to Australian patients, including from international laboratories as well as local university, research institute or hospital-based research laboratories.
- It was anticipated that the Stocktake tool developed will form the basis for similar future National surveys.

In summary, the purpose of the Stocktake was to provide an accurate estimate of the range and volumes of tests directed towards diagnosing and managing genetic disorders, which were completed across Australia during the 2016/17 financial year. Where possible, comparisons would be made with findings from the earlier surveys.

The scope of the Stocktake was to define:

- Types of laboratories and organisational departments within which genetic/ genomic testing is performed
- Referral pathways and clinical indications for tests
- Test volumes (per 100,000 people) for each state-based patient group (restricted to the groups of tests where state-by-state comparisons do not provide insights into the test volumes of any specific laboratory)
- Number and types of tests referred by recipient laboratories to international laboratories
- Scope of testing and the range of methods utilised
- Professional qualifications of laboratory staff
- Reporting (turnaround) times
- Funding sources
- Data storage infrastructure utilised and perceived adequacy of current infrastructure in meeting the NPAAC Requirements for the retention of Laboratory Records and Diagnostic Material (Sixth Edition 2013)
- Storage and sharing of details about locally identified genomic variants

4. Method

4.1 Description of Survey Instrument

A survey instrument was developed and then piloted by a small group of service providers representing all sectors. Development started with the 2011 survey instrument, which was modified substantially to address the various practical challenges that had been encountered by the participating laboratories and survey analysts, particularly the challenge of classifying the numerous varieties of genetic/ genomic investigations. Feedback on survey design was sought and incorporated from multiple representatives, including laboratories from the public, private and research sectors.
The final 2017 survey instrument consisted of five separate documents (Appendix B):

- Health Genomics Survey 2017 Laboratory Questions
- Health Genomics Survey 2017 Test Questions
- Health Genomics Survey 2017 Covering Letter
- Health Genomics Survey 2017 Guide for Participants
- Health Genomics Survey 2017 Confidentiality Agreement

The “Laboratory Questions” spreadsheet was designed to capture information on the category of laboratory, NATA accreditation, laboratory staffing, referral pathways for medical genetic testing, storage of genetic/ genomic data, and the tests referred to offshore laboratories.
The “Test Questions” spreadsheet was designed for laboratories to enter data about the tests performed during the 2016/17 financial year, including details about the tests; sample sources; reporting (turnaround) times, and funding. The “Test Questions” spreadsheet contained three tabs to accommodate the major test groups: constitutional cytogenetic and molecular (“cytomolecular”) genetic/ genomic tests; cancer-related cytomolecular tests, and biochemical genetics, including newborn bloodspot screening and maternal serum screening. This three-way separation, implemented as a result of insights gained during pilot testing, proved beneficial for laboratories entering data. The separation also proved useful for the analysis.

4.2 Participants

Aided by the overseeing groups, NATA and RCPAQAP, the RCPA’s Project Team identified Australian laboratories known to be offering genetic/ genomic testing services from the public, private or academic sectors. All public, private, and research laboratories known to have provided human genetic/ genomic tests for medical purposes in Australia during the 2016 to 2017 financial year were invited to participate. They included molecular, cytogenetic, and biochemical genetic testing for both heritable (constitutional) and cancer (somatic) genetic/ genomic changes. Medical testing of non-human genes (e.g. microbial genetic testing) and non-medical testing of human genes (e.g. paternity testing, forensic testing) were not included.

4.3 Confidentiality

Precautions were put in place to maintain the confidentiality and security of all information provided by laboratories. Raw data from laboratories, which were seen only by the Project Team, will be retained securely by the RCPA for the purposes of building a longitudinal dataset. It was agreed that only de-identified consolidated data (as referred to in the Confidentiality Agreement) would be made available to the Commonwealth, State and Territory Departments of Health, Project Committees, RCPA Executive, Fellows, Committees, or other professional bodies.

4.4 Data Collection

The survey was open to all laboratories for an eight-week period, which commenced on 19 February 2018 and ended on 23 April 2018. The invitation to participate was sent by email, accompanied with instructions on how to access the survey instrument. Laboratories were provided with individual access to ShareFile, enabling secure and streamlined submission of data. Follow-up

emails and telephone calls were made to laboratories to maximise the participation rate. Additional time was provided on request.

4.5 Data Cleansing, Aggregation and Analysis

The data submitted by individual laboratories were firstly reviewed by the Project Leads. When important uncertainties regarding data or missing information were identified, the Project Leads contacted relevant laboratory directors to gain clarification or secure the missing details. Any data that remained incomplete after this process was designated as “not provided”. Where possible, information available from the Commonwealth Department of Health about tests attracting Medicare reimbursements was presented alongside the equivalent data provided by laboratories. Otherwise, submitted data were accepted without additional independent validation.

```
. tab test_request if testrequest_recode==878

           Tests requested for analysis |      Freq.
----------------------------------------+-----------
                     Other (ALS C9orf72) |          1
Other - Familial amyotrophic lateral .. |          1
Other - Familial amyotrophic lateral .. |          1
                  Other - MND (C9ORF72) |          1
Other-Familial Amyotrophic Lateral Sc.. |          1
----------------------------------------+-----------
                                  Total |          5
```

The dropdown lists for Test Requests, Scope of testing (Test Target) and Test Methods proved useful for encouraging laboratories to use standard nomenclatures. Notwithstanding this benefit, 730 individual cytomolecular test items were listed. Manual review of the items revealed that a substantial proportion were pseudonyms (example on right).
After all pseudonyms were identified and aggregated, the numbers of test items reduced to 450 items.

Aggregation of data was performed at both national and state levels. State-level aggregation was determined by the originating source of each test request (i.e. the state-/ territory-of-origin of the sample) rather than the state/ territory of the testing laboratory. It should be noted however that details about the regional origins of samples were not available for ~16.3% of all cytomolecular tests.

Analysis was completed using tools available within Excel.

5. Results

5.1 Participation Rate

All Australian laboratories known to have offered human genetic/ genomic tests for medical purposes during the 2016 to 2017 financial year (1 July 2016 to 30 June 2017) were invited to participate (87 laboratories*). The overall participation rate was 95.4%, with four laboratories not responding.

5.2 Missing Data

Data submissions from some laboratories were incomplete. Among the 83 responding laboratories, 8 (9.5%) did not provide a range of details about accreditation status, clinical referrers, staffing and supporting infrastructure, and 6 laboratories (7%) did not provide information about tests completed. Additionally, all laboratories experienced varying difficulties providing all the information sought by the survey, most especially the details about referring clinicians, test clinical indications, reporting (turnaround) times and overseas referrals. These later issues were noted also in the 2011 survey.

5.3 Data Analysis Results

5.3.1 Laboratory and Test Characteristics

For the 2016/17 financial year, participating laboratories reported completing a total of 1,181,923 tests directed towards detecting or managing disorders with a primary genetic aetiology (constitutional- and cancer-related disorders).

The focus of the survey was to capture details of tests requested for the purposes of diagnosing constitutional genetic diseases; cancer; major fetal anomalies; newborn bloodspot screening for major inborn errors of metabolism and congenital hypothyroidism, as well as biochemical genetic investigations directed towards diagnosing early- or late-presenting inborn errors of metabolism. Also included were genetic investigations directed towards therapy selection, minimal residual leukaemic disease and transplant monitoring.

Genetic/ genomic tests, which included cytogenetic and molecular investigations, were grouped as either constitutional- or cancer (somatic)-related testing.

Biochemical tests included investigations directed towards the diagnosis of inborn errors of metabolism, maternal serum screening, and newborn bloodspot screening.

As biochemical testing directed towards identifying or diagnosing genetic disorders comprises measuring either analytes or enzyme activity levels, rather than genetic/ genomic investigations, these two divisions of testing are summarised separately in Tables 1 and 2 below.

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* *An additional laboratory that had performed ~500 constitutional tests was identified during the analysis phase. Although this laboratory quickly submitted completed questionnaires, it was not possible to include this data in the report. This experience, along with unanticipated discoveries of several small laboratories by the Project Leads in the earlier stages of the Project, raises the possibility of additional small laboratory service providers, which are unknown to NATA or the RCPA. It was notable that many of these small laboratories identified during the course of the survey were embedded within non-pathology departments of large research institute- or university-affiliated public-sector hospital complexes.*

Table 1: Laboratories offering genetic/ genomic (molecular/ cytogenetic) constitutional and/ or cancer investigations

Industry sector	No. of labs.
Public	38
Private	20
Catholic/ Schedule 3	3
Research	12
Total	**73**

Table 2: Laboratories offering biochemical investigations directed to screening for, or diagnosing genetic/ genomic disorders

Industry sector	No. of labs.
Public	5
Private	5
Total	**10**

5.3.2 Genetic/ Genomic Testing

The industry sectors delivering constitutional or cancer genetic/ genomic tests were: public (52% of participating laboratories), delivering 34.3% of the total number of tests; private (27.4%), delivering 63.3%; Catholic/ schedule 3 (4.1%), delivering 1.9%, and research (16.4%) delivering 0.4%. These proportions differ when constitutional- and cancer-related genetic/ genomic tests are considered separately. For example, while the private sector reported delivering 71% of constitutional tests, 60% of cancer-related tests were performed in the public sector (Figure 1 and Table 3).

Figure 1: Industry sectors delivering constitutional and cancer genetic/ genomic tests

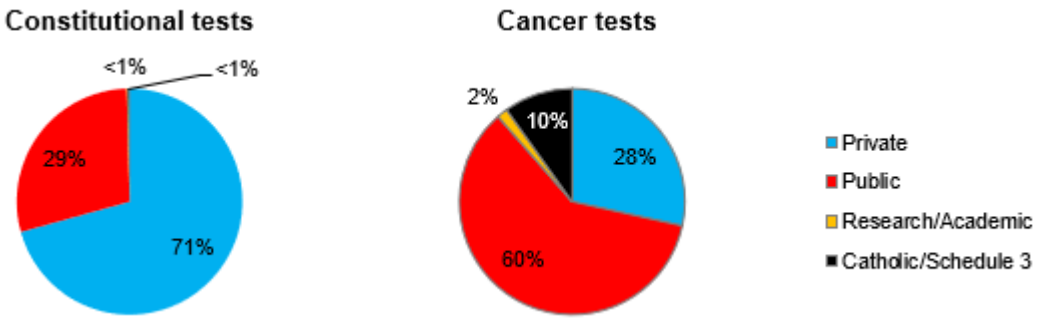


Table 3: Total number of tests across industry sectors

Number of tests (percentage of row total) by laboratory type					
Test category	**Private**	**Public**	**Research/ Academic**	**Catholic/ Schedule 3**	**Total**
Constitutional	385227 (70.68)	157494 (28.90)	916 (0.17)	1392 (0.26)	**545029**
Cancer	32737 (28.44)	69230 (60.14)	1776 (1.54)	11378 (9.88)	**115121**
Total	**417964 (63.32)**	**226724 (34.34)**	**2692 (0.41)**	**12770 (1.93)**	**660150**
Biochemical					
NBS	79230 (25.74)	228540 (74.26)	-	-	**307770**
MSS	120413 (82.07)	26306 (17.93)	-	-	**146719**
Diagnostic	15479 (23.01)	51805 (76.99)	-	-	**67284**

Abbreviations: MSS Maternal serum screening; NBS Newborn bloodspot screening

5.3.3 Biochemical Genetics/ Chemical Pathology Tests

Table 3 also summarises the relative contributions of the private and public sectors to biochemical tests, which were arranged for the following reasons:

- investigations directed towards newborn screening for the more common inborn errors of metabolism and congenital hypothyroidism;
- measurements of analytes/ enzymic functional activity to diagnose inborn errors of metabolism (Biochemical Genetics); and
- measurements of analytes relevant to the task of maternal serum screening for the common chromosomal aneuploidies and neural tube defects (Chemical Pathology).

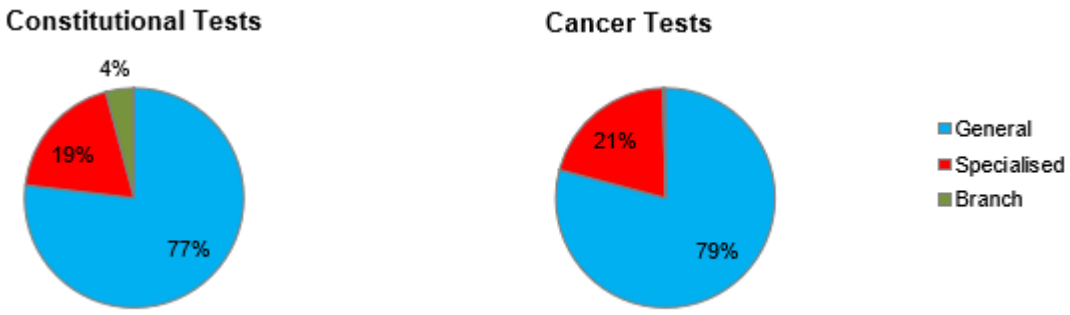
5.3.4 Laboratory Categories (NPAAC Classification)

Australian laboratories are classified by the 2007 NPAAC categories of general, branch, and specialised [2].

> *General* laboratories provide comprehensive multidisciplinary services under the direction, control and full-time supervision of staff who are expert in the group, or groups of services offered.
>
> A *Branch* laboratory is part of a general laboratory, but in a different geographic location.
>
> *Specialised* laboratories offer a limited range of services, which are supervised by a person with special relevant qualifications.

Seventy-eight percent of all genetic/ genomic and biochemical diagnostic tests were performed in general laboratories; 19% in specialised laboratories, and 3% in a branch laboratory. When constitutional and cancer-related genetic/ genomic tests are considered separately, there is some minor variation in the relative proportions of tests performed across these NPAAC laboratory categories (Figure 2).

Figure 2: Constitutional and cancer genetic/ genomic tests across NPAAC laboratory categories



5.3.5 Laboratory Accreditation

Seventy-two of 80 laboratories (90%) that provided accreditation details indicated that they were accredited (Table 4). Among the 8 non-accredited laboratories, one was in the service sector and the remaining 7 were research laboratories. Non-accredited laboratories performed 0.14% of all tests.

Table 4: NATA accreditation

NATA Status	Number of laboratories			Percent
	Service	Research	Total	
Already NATA accredited	67	5	72	**90**
Not NATA accredited	1	7	8	**10**
Total	**68**	**12**	**80**	**100**

The 2011 survey, which targeted only NATA accredited laboratories, received responses from 39 laboratories. The higher number of accredited laboratories that contributed to the current survey represents an 85% increase over the 5½ year interval between surveys.

5.3.5.1 Accreditation for Massively Parallel Sequencing

Of the 72 accredited laboratories, 59 were accredited for genetic/ genomic testing, of which 32 (54.2%) had an accreditation scope that included massively parallel sequencing (MPS).

Among the 32 laboratories accredited for MPS, 22 (69%) had achieved NPAAC's upgraded 2017 requirements. A further six laboratories indicated they were progressively addressing NPAAC'S revised requirements for MPS validation, staff training and supervision.

5.3.6 Interstate Transfer of Samples

The proportions of samples being transferred interstate for cytogenetic, molecular and biochemical genetic testing (excluding maternal serum screening (MSS) and newborn bloodspot screening (NBS) over the past decade are demonstrated below (Figure 3).

In contrast to the reported proportions of samples transferred interstate for testing in 2006 and 2011, the data submitted on this occasion revealed that at least 23% (123,328) of constitutional genetic/ genomic tests and 12% (13,974) of cancer-related tests were performed on samples transferred across state or territory borders.

It is important to note on this occasion that the state- or territory-of-origin of samples was not provided for 16.3% of samples (see section 5.3.6.1 below).

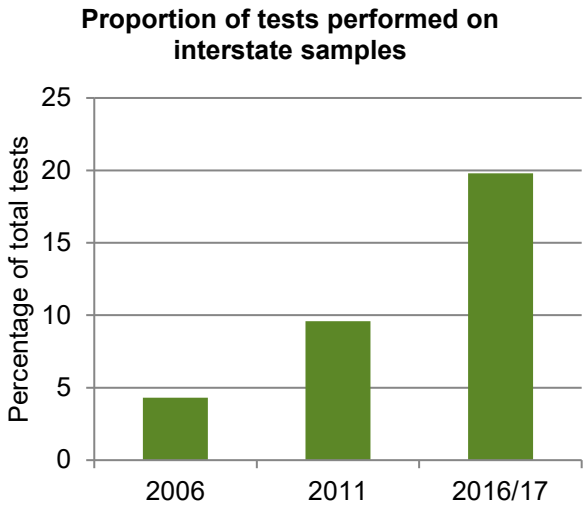


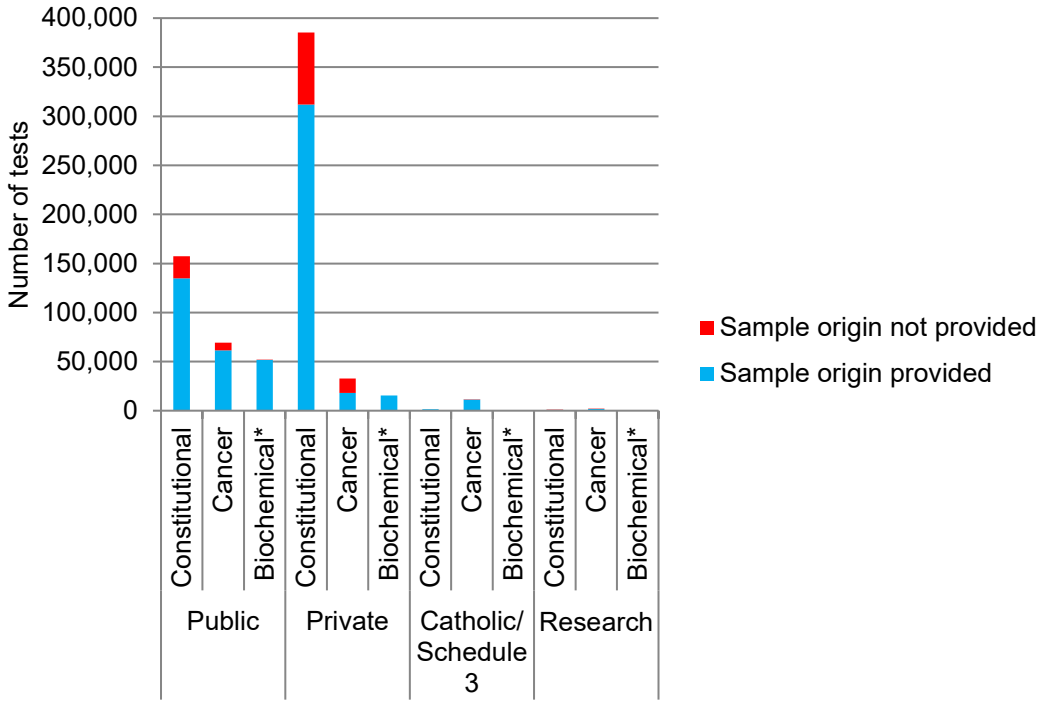
Figure 3: Interstate sample testing (2006, 2011 and 2016/17)

Data include cytogenetic, molecular and biochemical diagnostic tests (MSS and NBS are excluded).

5.3.6.1 State-/ Territory-of-Origin of Samples – Missing Details

Among the 727,434 constitutional, cancer and biochemical genetic diagnostic tests reported by laboratories, details about the regional origins of samples were not provided for 118,529 cases (16.3%). To provide some insight into whether these missing details may have distorted the above estimate of the proportions of interstate transfers, the total numbers of samples tested within the categories of constitutional, cancer and biochemical genetics (diagnostic) with and without details about the source of samples were listed for each industry sector (Figure 4).

Figure 4: Missing details about state-/ territory-of-origin of samples



**Data include biochemical diagnostic tests (MSS and NBS are excluded).*

Missing details about the regional source of samples occurred among all sectors; however, the private sector accounted for 74% of all cases where the information was not provided. To some extent, this reflects the overall rate of testing now provided by private laboratories. It is possible that information about the regional origins of samples may have been regarded as commercially sensitive and that the most recent estimate of the proportion of interstate transfers (Figure 3) is an under-representation.

5.3.7 Outsourcing of Wet Work

Participants in the 2016/17 survey reported that 2,837 samples were transferred to another laboratory within the same state for wet work, with sequence data files subsequently returning for analysis and reporting. A further 467 samples were forwarded to interstate laboratories for wet work, again with the raw data being returned for analysis and reporting. Similarly, 602 samples were transferred overseas for wet work with the overseas laboratories dispatching sequence data files back for local analysis and reporting (these later sample numbers are included in Table 5 below).

5.3.8 International Transfers

5.3.8.1 Incoming Tests

A total of 8,386 tests were performed in 2016/17 by Australian laboratories on samples received from overseas laboratories (Table 5). The predominant tests sought for incoming samples were comprehensive HLA genotyping; testing for cancer-related disorders; pre-conception carrier screening; whole exome sequencing, and MPS-based panel testing.

Table 5: Numbers of tests received from or sent to international laboratories

Total no. incoming tests	Total no. outgoing tests
8386	3625

5.3.8.2 Outgoing Tests

Laboratories reported referring 3,625 samples to international laboratories for testing in 2016/17, compared to 2,766 in 2011. A breakdown of the test requested is provided in Table 6.

Table 6: Tests referred overseas

Test Request	No. of tests
Non-invasive prenatal testing	1537
Panel – cardiac disorders	244
Panel – intellectual impairment/ autism	203
Panel – epilepsy syndromes	105
Preconception carrier screening (expanded)	103
Panel – retinal dystrophy	81
Panel – hereditary hearing loss (OtoSCOPE)	28
Panels (various)	556
Neurofibromatosis single gene/ panel	36
Single genes/ variants (various)	318
Pre-implantation genetic diagnosis (various)	25
Whole exome sequencing	302
Whole genome sequencing	31
Research (various)	56

Personal communication between the Project Leads and a range of specialist medical practitioners, particularly obstetricians, clinical geneticists, biochemical geneticists, endocrinologists, haematologists and anatomical pathologists, revealed the existence of an additional substantial flow of samples being sent directly overseas via independent couriers. As these referrals bypassed laboratories contributing to the survey, information about these additional outgoing test requests was not captured.

Additionally, the Project Leads became aware of an overseas laboratory that has an Australian-based sample receipt and forwarding facility. This facility declined its invitation to participate in the stocktaking survey.

5.3.8.3 Reported Experience of Test Referrals from a Single Tertiary Paediatric Centre

A valuable insight into the nature of "sendaway" referrals, a proportion of which would not have been recorded in this survey, comes from Laboratory Services, Royal Children's Hospital (RCH), Melbourne. This service provides a broad range of pathology services. It is also responsible for referring samples for testing to third-party providers. Notably, the budget for pathology testing, including genetic/ genomic testing, sits with Laboratory Services rather than devolved to clinical units.

The Director of RCH Laboratory Services explained that in response to a phase of exponential growth in demand for genetic/ genomic testing services, with associated rising costs and prolonged delays in results returning from external providers, genetic test requests were internally audited in 2016. An important outcome of the audit was the employment of a Laboratory Genetic Counsellor (GC), who now contributes to the review of test requests and, where necessary, contacts referring clinicians to ensure that the investigations are optimally targeted towards addressing the clinical issues prompting the requests.

The GC assists in the selection of accredited laboratories, ensuring that the chosen laboratories can deliver results within a clinically-relevant time frame. The GC also liaises with the laboratory staff responsible for managing the sendaway referrals and results. Additionally, high cost test requests are reviewed at a monthly review panel meeting attended by the laboratory director, the laboratory GC, the laboratory quality manager, a clinical geneticist and other specialist clinicians, as required.

In the 12-month period from December 2016 to December 2017, which partially overlaps the time interval for the survey, approximately 400 samples (~35/ month; range 20-47) were referred to a range of local, interstate and international laboratories. Data available for the 3 year interval 2015-2017 show that more than half of all genetic/ genomic test requests were referred directly offshore, which means they would not have been recorded in this survey.

It is uncertain whether extrapolations for the rest of the country can be made from this single anecdotal experience. It should be noted that the clinical profile of RCH reflects its role as a secondary and tertiary provider of paediatric and adolescent services to residents of Melbourne's northern and western suburbs; as well as specialist paediatric services spanning Victoria, Tasmania, southern NSW and parts of South Australia. It is the designated state-wide provider of services for paediatric trauma, rehabilitation and forensic medicine. It is also an Australia-wide quaternary referral centre for complex cardiac surgery and organ transplantation. Overall, it seems possible that this experience may represent up to a quarter or a third of paediatric/ adolescent referrals from across the country.

In summary, it would appear that the survey number in Table 5 of 3,625 samples referred to international centres for testing in 2016/17 substantially underestimates the true picture.

5.3.9 Tests per Capita, by State/ Territory

To address the requirement of providing insights into equity of services and access, details provided by laboratories about the state-/ territory-of-origin of tests were summarised as overall numbers of tests per capita for the 2011 and 2016/17 surveys (Table 7), as well as numbers of tests within each of the major test categories per capita for each state and territory (Table 8).

The data summarised within these tables should be considered with the following four caveats in mind:

1. There are differences in how a 'single test' was defined between the 2011 and 2016/17 surveys. In the 2011 survey, tests that included multiple targets were generally counted as separate tests. For example, an aneuploidy screen that included analysis of chromosomes 13, 18 and 21 was listed as three separate tests in the 2011 report, whereas such 'panel' tests have been counted as a single test in the 2016/17 report.

2. Analysis for the 2011 survey was based on the state/ territory location of laboratories, rather than the state-/ territory-of-origin of samples.
3. During the 5 ½ year interval since the 2011 survey, the proportion of samples transferred across state and territory borders has grown from 11%, overall, to 23% for constitutional genetic/ genomic tests and 12% for cancer-related tests (19.8% overall).
4. Details about the state/ territory-of-origin of samples were not available for approximately 118,500 tests (~16.3%) of samples.

To ameliorate partially the effects of missing details about the geographic origins of samples, for public-sector laboratories, it was assumed that the state-of-origin was the state in which the testing laboratory was located. Notwithstanding this assumption, it was known that a small proportion of the work done in public sector laboratories was on samples forwarded across State boundaries.

Table 7: Test numbers per capita, by state/ territory

				Per 100,000 population		
State/ Territory	2016/17 Tests	2011 Tests	% change	2016/17 Tests	2011 Tests	% change
ACT	12775	2356	442%	3110	640	386%
NSW	189381	136869	38%	2410	1890	28%
NT	1241	-	-	500	-	-
QLD	118124	143281	-18%	2400	3170	-24%
SA	49616	52617	-6%	2880	3200	-10%
TAS	11544	1713	574%	2220	330	573%
VIC	184208	167797	10%	2910	3010	-3%
WA	50163	75109	-33%	1940	3150	-38%
Total	**704980**	**579742**	**22%**	**2870**	**2610**	**10%**

Notes:
1. 2011 population data from Preliminary 2011 Census data, ABS. 2016/17 data from 2016 Census.
2. 2016/17 newborn bloodspot screening, maternal serum screening, HLA typing and tests performed in research laboratories were excluded to allow comparison with 2011 data.
3. The Total test number is inclusive of samples where geographic origin was not provided.

The 2011 survey, which excluded HLA-typing, maternal serum screening and newborn bloodspot screening, reported 579,742 tests performed during the 2011 calendar year. Exclusion of the same test categories gives a total of 704,980 tests for 2016/17, which represents a 22% increase between the two surveys. After correcting for regional population growth, the change equates to a 10% increase in tests per capita. It is expected that this figure substantially underestimates the growth of genetic/ genomic testing. The apparent low growth in test volumes may be largely explained by differences in the definition of a single test between the two surveys (see caveat 1, above), particularly as technological advances have led to an emerging trend towards the utilisation of single large gene panel tests in lieu of multiple sequentially-ordered investigations.

When the percentage changes for each state and territory are considered, several notable differences are evident, particularly for Tasmania, the ACT, South Australia, Queensland and Western Australia. The extent of the differences suggests that some or all of the above caveats may

apply and that care needs to be taken when considering the data from the viewpoint of gaining insights into equity of services and access.

Table 8: Test categories - state/ territory per capita numbers

State/ Territory	Test categories	No. of tests	No. per 100,000 population
ACT			
	Constitutional	10759	2622.22
	Cancer	2293	558.86
	Biochemical	29	7.07
	MSS	4312	1050.94
	NBS	5152	1255.66
NSW			
	Constitutional	145451	1850.27
	Cancer	30428	387.07
	Biochemical	18098	230.22
	MSS	47938	609.82
	NBS	98228	1249.55
NT			
	Constitutional	658	267.37
	Cancer	283	114.99
	Biochemical	305	123.93
	MSS	2198	893.11
	NBS	3326	1351.46
QLD			
	Constitutional	78018	1583.01
	Cancer	23232	471.38
	Biochemical	17193	348.85
	MSS	17766	360.48
	NBS	58409	1185.14
SA			
	Constitutional	31316	1816.95
	Cancer	10914	633.23
	Biochemical	8055	467.35
	MSS	17295	1003.45
	NBS	21199	1229.96
TAS			
	Constitutional	8934	1715.18
	Cancer	2107	404.51
	Biochemical	718	137.84
	MSS	3819	733.19
	NBS	5737	1101.41
VIC			
	Constitutional	146005	2308.89
	Cancer	27533	435.40
	Biochemical	13783	217.96
	MSS	39864	630.40
	NBS	79230	1252.92
WA			
	Constitutional	41376	1603.50
	Cancer	5343	207.06
	Biochemical	8478	328.56
	MSS	13527	524.23
	NBS	36300	1406.78

Abbreviations: MSS Maternal serum screening; NBS Newborn bloodspot screening
Notes: As described in the caveats above, the state-/ territory-of-origin of the sample was not provided for approximately 118,500 tests. For public laboratories, the missing states-of-origin of samples were categorised as the states in which the testing laboratory was located.

5.3.10 Pregnancy-Related Screening Tests

For the purposes of screening for major fetal anomalies, prenatal tests include maternal serum screening and ultrasound; the goals of which are to identify women with pregnancies at high risk of major chromosomal abnormalities or birth anomalies such as neural tube defects.

Several screening options are available, including first-trimester (9-13+ weeks) and second-trimester (14-18 weeks) screening. In recent years, “non-invasive” prenatal screening (NIPS) has emerged and there is a growing trend for this to supersede the earlier first- and second-trimester screening methods. NIPS involves collecting a maternal serum sample from 10 weeks gestation onwards, from which cell-free fragments of DNA from the pregnancy are isolated and screened for evidence of the more frequently occurring major fetal chromosomal anomalies.

The survey findings for pregnancy-related screening tests (Table 9) reveal that screening tests, either first trimester or NIPS, are arranged for approximately two thirds of pregnancies in Australia. The data reveal also the proportionately much lower level of maternal second trimester screening.

Table 9: Pregnancy screening test categories

Test categories	No. of tests
Maternal first trimester screening (biochemical)	140805
Maternal second trimester screening (biochemical)	5914
Non-invasive prenatal screening (DNA)	55789

5.3.11 Genetic/ Genomic Testing – Referral Sources

The most common referral source for genetic/ genomic testing in 2016/17 was General Practitioners (27.7% of test requests) (Table 10). Obstetricians/ Fertility/ Fetal Medicine Specialists (21.1%) and Pathologists (15.4%), particularly Haematologists (8.9%), were the next most frequent referring groups. These were followed by Clinical Geneticists and Oncologists, who accounted for 6.6% and 5.4% of all test requests, respectively.

Table 10: Referral sources

Referral Sources	No. of referrals	Percentage
General Practitioners	170318	27.65
Obstetricians/ Fertility Specialists/ Fetal Medicine Specialists	129930	21.09
Paediatricians	50004	8.12
Clinical Geneticists	40579	6.59
Oncologists	33238	5.40
Neurologists	9573	1.55
Endocrinologists	7646	1.24
Cardiologists	2324	0.38
Pathologists (Total of the five subgroups below)	94650	15.36
Haematologists	*55072*	*8.94*
Anatomical Pathologists (including Forensic, Perinatal and Paediatric)	*15165*	*2.46*
General Pathologists	*14749*	*2.39*
Immunologists	*8853*	*1.44*
Chemical Pathologists	*811*	*0.13*
Other Medical Practitioner Groups	*77772*	12.62
Total no. medical practitioner referrals	**616034**	**100.0**

Note: The numbers and percentages in italics are for each of the pathology subgroups.

5.3.12 Genetic and Genomic Testing – Clinical Referral Categories

The most common reasons for testing were for diagnostic purposes in patients with symptoms of a constitutional genetic condition (55% of test requests) and in patients with cancer (12%) (Table 11). The next most common referral category was prenatal screening of maternal blood for major chromosomal anomalies (NIPS) (8.5%). The remaining quarter of genetic/ genomic test requests were spread over the wide range of clinical referral categories listed in the table.

Diagnostic and screening purposes, which were merged in the 2011 survey, represented the most common reason for testing in the previous survey. However, accurate comparison cannot be made with the 2011 survey due to differences in the definition of a single test between the two surveys, as described in Section 5.3.9.

Table 11: Clinical referral categories

Clinical referral categories [1]	No. of tests	Percentage
Subcategories		
Diagnostic/ family cascade testing		
Symptomatic patient (constitutional)	361839	55.23
Symptomatic patient (cancer)	77854	11.88
Family segregation analysis (to assist variant classification) [2]	4194	0.64
Familial cascade testing of a known pathogenic variant	14626	2.23
Carrier testing (autosomal and X-linked recessive disorders)	15267	2.33
Therapy selection/ monitoring		
Tumour sample genotyping	14243	2.17
Minimal residual disease/ transplant monitoring	18024	2.75
HLA typing (allograft-related comprehensive sequencing)	9607	1.47
Pharmacogenomic testing (constitutional)	18598	2.84
Prenatal		
Testing of fetal tissues [3]	12464	1.90
Maternal blood (fetal aneuploidy screening)	55789	8.52
Maternal blood (fetal DNA Rhesus screening)	57	0.01
Pre-implantation genetic testing		
Aneuploidy screening	11981	1.83
High risk monogenic disease testing	1129	0.17
Population screening		
Newborn bloodspot screening (molecular genetic component)	2571	0.39
Genetic disease detection (population risk)	17033	2.60
Recessive mutation carrier screening (population risk)	19874	3.03

1. *The referral category was provided for 99.2% of tests (data were missing for 5,000 tests).*
2. *Familial cascade testing of known pathogenic variants for presymptomatic or predictive diagnostic testing. This does not include carrier testing for recessive/ X-linked disorders. Independent sample confirmatory tests are included in the total numbers.*
3. *Testing of fetal tissues (amniocentesis, chorionic villus sampling).*

5.3.13 Genetic and Genomic Tests – Nature of Testing

Genetic and genomic tests for both constitutional- and cancer-related disorders can be viewed from several perspectives, including levels of test targeting, genomic resolution, method selection and the potential clinical relevance of test findings.

5.3.13.1 Cytogenetic / Molecular Tests

To allow comparisons with the 2006 and 2011 survey findings, all genetic/ genomic tests for constitutional disorders and cancer were grouped as cytogenetic or molecular tests. The cytogenetic category comprised both microscopy-based karyotyping and FISH.

Overall, cytogenetic testing represented 15% of all constitutional- and cancer-related tests. This represents a substantial decline from 33%, which was documented in the 2011 survey.

When constitutional- and cancer-related tests are separated, it can be seen that the decline is more apparent in the constitutional testing sector (Figure 5). To provide further insights into the changing overall volumes of molecular and cytogenetic testing across Australia over the past decade, the total numbers of these tests reported in each of the three surveys are also presented (Figure 6).

Figure 5: Cytogenetic and molecular tests

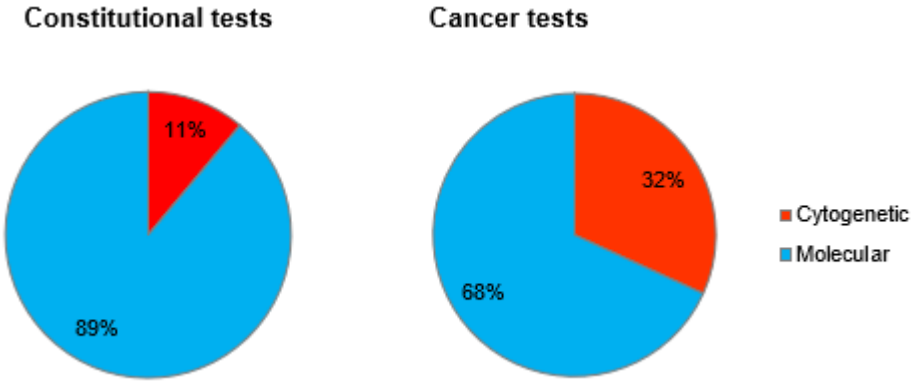
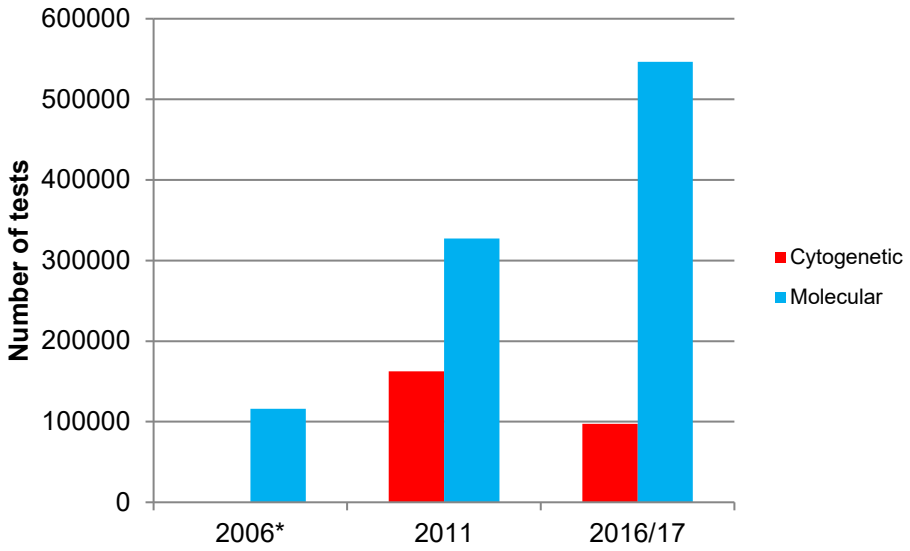


Figure 6: Cytogenetic and molecular test volumes (2006, 2011 and 2016/17)[1]



[1] HLA typing and tests performed in research laboratories have been excluded from this figure to allow comparison with previous survey data.
**No data are available for cytogenetic tests from 2006 as this was outside of the scope of the 2006 survey.*

*Constitutional disorder-related testing**
Among 545,029 tests performed for constitutional conditions in 2016/17, 484,455 were categorised as molecular and 60,574 were cytogenetic. This contrasts with approximately 403,500 constitutional tests performed in 2011, of which ~ 283,400 were molecular and 120,100 were cytogenetic. The growth in molecular testing during this period was 71%, while the decline in cytogenetic tests was 50%.

*Cancer-related testing**
Among 115,121 cancer-related tests performed in 2016/17, 78,510 were categorised as molecular and 36,611 were cytogenetic. This contrasts with approximately 83,400 cancer-related genetic tests performed in 2011, of which ~ 41,200 were molecular and 42,200 were cytogenetic. The observed growth in molecular testing during this period was 90%, while the total number of cytogenetic tests fell by approximately 13%.

** Please note, while comparative test volumes for 2011 and 2016/17 have been provided, the definition of a "single test" differs between the two surveys (described in Section 5.3.9).*

5.3.13.2 Test Complexity-associated Categories

Genetic/ genomic testing for constitutional disorders or cancer can also be stratified into categories that take some account of the various levels of technical or interpretive complexity associated with testing.

The complexities within the test categories itemised in Table 12 escalate from a targeted assay directed towards addressing whether a specific genetic variant is present or absent, through to untargeted screening of a patient's complete genome for what may prove to be a previously unknown disease-causing genetic change.

For constitutional tests, most investigations (78.3%) were targeted to determine whether a predefined genomic variant(s) was present or absent. For cancer-related testing, most assays were also directed towards determining the presence or absence of predefined variants (71.1%); however, in situ hybridisation (ISH) methods contributed substantially to the percentage (Table 12).

The number of ISH-type tests used in the cancer arena was more than three times higher than the number performed for constitutional disorders. However, because of the higher overall volume of constitutional testing, the difference in the percentage contributions of ISH-type analysis to cancer- and constitutional-related testing was more striking – 14.3% and 0.9%, respectively. Similarly, karyotyping contributed proportionately more to cancer-related testing, reflecting its ongoing utility, particularly for leukaemia diagnosis, therapy selection and prognosis.

Chromosomal microarray analysis, in contrast to karyotyping and ISH-type analysis, is performed ~25 times more frequently in the constitutional arena than for cancer testing.

Comparisons of the absolute numbers and associated percentage contributions to constitutional- and cancer-related testing for each of the other test categories listed in Table 12 reveal further large differences, each of which are worthy of considerations that go beyond the scope of this summary overview.

Table 12: Test complexity-associated categories: constitutional and cancer

Test Category	Constitutional		Cancer	
	No. of Tests	Percent	No. of Tests	Percent
Targeted testing for presence/ absence of predefined genomic variation (molecular)	421599	77.35	65319	56.74
Targeted testing for presence/ absence of predefined genomic variation (FISH/ ISH)*	4961	0.91	16509	14.34
Targeted screening for undefined variants in a single gene	6608	1.21	86	0.07
Targeted screening for undefined variants in fewer than 50 genes	13959	2.56	9139	7.94
Targeted screening for undefined variants in 50 or more specified genes	3124	0.57	2351	2.04
Untargeted screening of all chromosomes (karyotyping)	55613	10.20	20102	17.46
Untargeted higher-resolution screening of all chromosomes (microarray)	38358	7.04	1436	1.25
Untargeted screening of whole exome	461	0.08	0	0
Untargeted screening of whole genome	346	0.06	0	0
Gene expression studies	0	0	179	0.16
Total	**545029**	**100**	**115121**	**100**

**(F)ISH (Fluorescent) in situ hybridisation*

5.3.14 Test Volumes

The total numbers of constitutional- and cancer-related tests are detailed in Appendix A. To aid the task of reviewing these data, the tests are listed both alphabetically and by total numbers (Tables 41 & 42). Otherwise, all tests with volumes exceeding 10,000 are listed below (Table 13).

The highest volume tests reported in 2011 were *HFE, F5, F2, CFTR, MTHFR, BCR-ABL1, JAK2*, chromosomal karyotyping, aneuploidy screening and HLA typing, all of which are represented among the 2016/17 high-volume test list.

Table 13: Higher volume tests

Constitutional*		Cancer*	
Test name	**Volume**	**Test name**	**Volume**
Hereditary haemochromatosis, *HFE*	75,170	Chromosomal karyotype	20,102
Aneuploidy Screening (non-invasive prenatal)	55,789	Leukaemia, t(9;22) *BCR-ABL1*	18,715
Chromosomal karyotype	55,613	MDS/ MPN/ Leukaemia, *JAK2*	16,343
Factor V Leiden, *F5*	41,815		
Prothrombin, *F2*	40,815		
Untargeted chromosomal microarray	38,358		
HLA B27	36,615	**Biochemical genetics***	
HLA DR/DQ	20,403	**Test name**	**Volume**
Fragile X, *FMR1* triplet repeat	17,832	Amino acids (blood, urine, CSF)	15,562
Cystic fibrosis, *CFTR*	17,126	Organic acids (urine)	12,621
MTHFR	16,803	Glycosaminoglycan screen (urine)	11,758
Alpha-thalassaemia	12,092		
Aneuploidy Screening (pre-implantation genetic testing)	11,981		
HLA (comprehensive sequencing)	11,470		

** Investigations with more than 10,000 tests performed over the 2016/17 financial year are provided. Newborn and maternal serum screening have been excluded.*

As many of the tests in Table 13 are associated with a Medicare rebate, a further comparison has been made against published Medicare statistics (Table 14) [3]. Review of the numbers of Medicare-funded tests reported by laboratories reveals several inconsistencies between the number of services per capita reported by laboratories and the equivalent details available from Medicare. It may be relevant that the sources of funding were not provided for 18% of constitutional tests, 24% of cancer tests and 4% of biochemical diagnostic tests (excluding newborn bloodspot screening and maternal serum screening). The furthest right column of Table 14 assumes that, where funding details were not provided by participating laboratories, these tests were also Medicare-funded.

Table 14: Medicare services per capita (high volume assays)

Item	Description	Services per 100,000 population				
		MBS data			2016/ 2017 Survey data	
		2016/ 2017	2011	% change	Funding details provided	Funding gaps also assumed as Federal
Constitutional						
73317	Detection of C282Y in the *HFE* gene in a patient with consistently elevated TS or SF, or a first degree relative with haemochromatosis or homozygosity for C282Y/ relevant compound heterozygosity	257	250	3%	209	283
73287	The study of the whole of every chromosome by cytogenetic or other techniques, performed on 1 or more of any tissue or fluid except blood	45	78	-42%	Karyotype: 191 Microarray: 104	Karyotype: 214 Microarray: 136
73289	The study of the whole of every chromosome by cytogenetic or other techniques, performed on blood	198	131	51%		
73292	Analysis of chromosomes by genome-wide microarray in a person with developmental delay, intellectual disability, autism, or at least two congenital abnormalities	66	33	100%		
73308	Characterisation of the genotype of a patient for Factor V Leiden gene mutation, or detection of the other relevant mutations in the investigation of proven venous thrombosis or pulmonary embolism	100	74	35%	100	144
73311	Characterisation of the genotype of a person who is a first degree relative of a person who has proven to have 1 or more abnormal genotypes under item 73308	16	21	-24%	2	2
73300	Detection of a mutation of the *FMR1* gene	43	26	65%	39	48
73320	Detection of HLA-B27 by nucleic acid amplification	109	31	252%	63	137
71147	HLA-B27 typing	229	177	29%		
71151	Tissue typing for HLA-DR, HLA-DP and HLA-DQ Class II antigens - phenotyping or genotyping of 2 or more antigens	165	87	90%	83	83
Cancer						
73287	The study of the whole of every chromosome by cytogenetic or other techniques, performed on 1 or more of any tissue or fluid except blood	45	78	-42%	Karyotype: 55 Microarray: 2	Karyotype: 66 Microarray: 4
73290	The study of the whole of each chromosome by cytogenetic or other techniques, performed on blood or bone marrow, in the diagnosis and monitoring of haematological malignancy	35	29	21%		
73314	Characterisation of gene rearrangement or the identification of mutations within a known gene rearrangement, in the diagnosis and monitoring of patients with laboratory evidence of AML, APML, ALL, or CML	60	24	150%	63	86
73315	A test described in item 73314, if rendered by a receiving approved pathology practitioner	14	18	-22%		
73325	Characterisation of mutations in *JAK2*, *MPL*, or both genes, in a patient with clinical and laboratory evidence of PV or ET.	52	8	550%	35	60

AML Acute myeloid leukaemia; APML Acute promyelocytic leukaemia; ALL Acute lymphoid leukaemia; CML Chronic myeloid leukaemia; ET Essential thrombocythaemia; PV Polycythaemia vera; TS Transferrin saturation; SF Serum ferritin

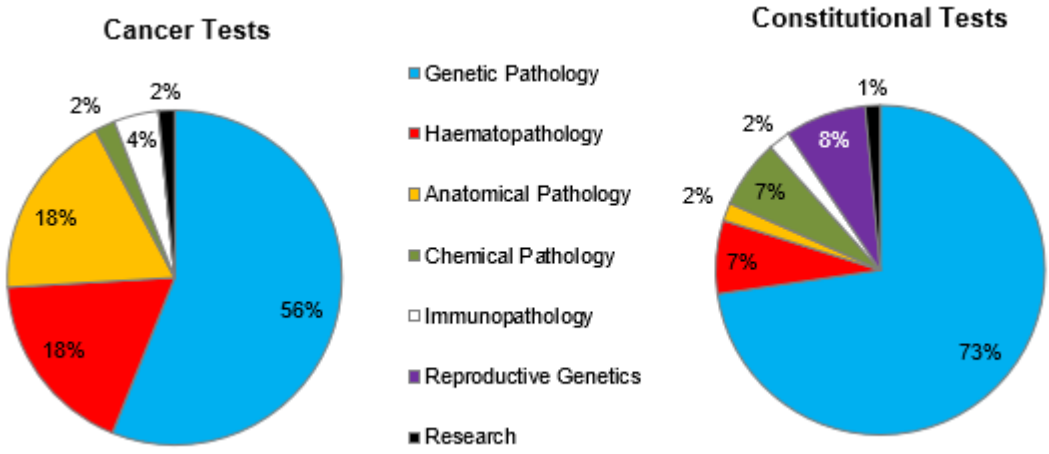
5.3.15 Discipline-based Genetic/ Genomic Testing

Approximately three quarters of all constitutional genetic/ genomic tests (72.7%) were performed within departments identifying as Genetic Pathology (Figure 7). The disciplines of Reproductive Genetics, Chemical Pathology and Haematology contributed to the bulk of the remaining

constitutional tests. Other contributing disciplines were Anatomical Pathology and Immunology, as well as research-based laboratories.

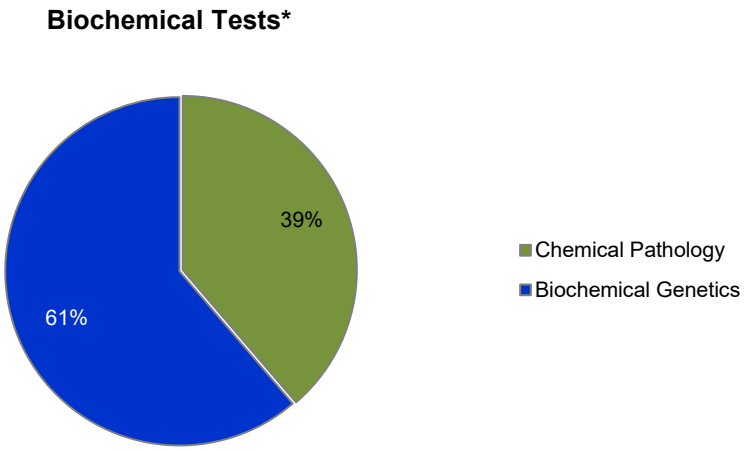
Fifty six percent of cancer-related testing was performed within Genetic Pathology-identifying laboratories. These tests, combined with those performed in Anatomical Pathology (18.1%) and Haematology (18.0%), contributed to more than 90% of cancer-related testing. The other disciplines contributing to cancer-related testing were Immunopathology and Chemical Pathology. Research-based laboratories contributed to 2% of cancer tests, in contrast to 1% for constitutional tests.

Figure 7: Distribution of constitutional- and cancer-genetic/ genomic tests across laboratory disciplines



For biochemical genetic diagnostic analytes and enzymic assays, 61% were performed in Biochemical Genetic laboratories and the remainder in Chemical Pathology services (Figure 8).

Figure 8: Distribution of biochemical tests across laboratory disciplines



**Maternal serum screening and newborn bloodspot screening excluded.*

5.3.15.1 Complexity-associated Categories across Pathology Disciplines

For each test category within constitutional- and cancer-related testing, the percentage contributions from each laboratory discipline are listed below (Table 15).

Notable features within the table are –

- Targeted molecular testing for predefined variants: all laboratory disciplines were involved in this testing.
- FISH-based analysis: Genetic Pathology and Anatomical Pathology predominant.
- Gene panel screening (2-49 genes): Genetic Pathology, Anatomical Pathology and Immunology predominant.
- Gene panel screening (50+ genes): Genetic Pathology and Anatomical Pathology predominant.
- Chromosomal karyotyping: Genetic Pathology, Haematology and Reproductive Genetics predominant.
- Chromosomal microarray analysis: Genetic Pathology and Haematology predominant.
- Exome/ Genome screening: Genetic Pathology and research teams predominant.
- Gene expression studies: Performed by Genetic Pathology, Chemical Pathology and research teams.

Table 15: Constitutional and cancer tests by test category and laboratory department

Test categories	Constitutional/ Cancer	Total no. of tests	Laboratory Disciplines (% total tests performed in each discipline)						
			Genetic Pathology	Haematology	Anatomical Pathology	Chemical Pathology	Immunology	Reproductive Genetics	Research
Targeted: predefined variant(s) (molecular)	Constitutional	**421599**	72.4	8.5	1.5	8.4	1.6	5.9	1.7
	Cancer	**65319**	53.7	25	18.2	1.3	-	N/A	1.8
Targeted: predefined variant(s) (FISH)	Constitutional	**4961**	94.6	-	0.4	-	-	4.9	-
	Cancer	**16509**	74.7	1.1	24.1	0.1	-	N/A	-
Single gene screening	Constitutional	**6608**	62.7	0.8	-	-	1.9	30.2	4.3
	Cancer	**86**	4.7	-	82.6	-	-	N/A	12.8
2 - 49 genes	Constitutional	**13959**	47.3	0.6	11.3	0.5	36.0	3.9	0.4
	Cancer	**9139**	9.4	-	19.1	13.8	54.7	N/A	3.1
50+ genes	Constitutional	**3124**	39.7	-	41.0	6.4	-	5.1	7.7
	Cancer	**2351**	10.6		78.7	-	-	N/A	10.6
Chromosome screening (karyotyping)	Constitutional	**55613**	66.3	4.2	0.6	1.1	-	27.9	-
	Cancer	**20102**	73.7	20	6.3	-	-	N/A	-
Chromosome screening, higher res. (microarray)	Constitutional	**38358**	95.3	2.5	0.8	0.9	-	0.6	-
	Cancer	**1436**	83.6	14.8	1.6	-	-	N/A	-
Untargeted screening of whole exome	Constitutional	**461**	74.2	-	-	-	-	-	25.8
	Cancer	-	-	-	-	-	-	N/A	-
Untargeted screening of whole genome	Constitutional	**346**	93.4	-	-	-	-	-	6.6
	Cancer	-	-	-	-	-	-	-	
Gene expression studies	Constitutional	-	-	-	-	-	-	-	-
	Cancer	**179**	5.6	-	-	67.6	-		26.8

5.3.15.2 Test Complexity-associated Groupings across Industry Sectors

A breakdown of the numbers of private, public, Catholic/ schedule 3 and research laboratories offering tests within each complexity-related category is provided below (Table 16).

Notable features within the table are –

- Private- and public-sector laboratories offered genetic/ genomic tests within virtually all test categories. The exceptions are exome sequencing, which was provided by a limited number of public laboratories and one research group, and whole genome sequencing, which was provided by one private laboratory and one research team.
- A limited number of Catholic/ schedule 3 laboratories offered testing within the categories of targeted analysis for predefined variants, chromosomal karyotyping and microarray analysis.
- Genetic/ genomic testing services provided by research teams were delivered using both long-established and newer genetic/ genomic technologies.

Table 16: Distribution of genetic / genomic test complexity-associated groups across industry sectors (constitutional- and cancer-related testing)

Test groups	No. of Labs	Laboratory Type (number offering each test category)			
		Private	Public	Catholic/ Schedule 3.	Research/ Academic
Targeted: predefined variant(s) (molecular)	52	14	31	1	6
Targeted: predefined variant(s) (FISH)	22	7	11	4	-
Single gene screening	29	9	16	-	4
2 - 49 genes	25	7	16	-	2
50+ genes	11	3	5	-	3
Chromosome screening (karyotyping)	19	8	9	2	-
Chromosome screening, higher res. (microarray)	20	10	9	1	-
Exome	5	-	4	-	1
Genome	2	1	-	-	1
Gene expression studies	3	1	1	-	1

5.3.15.3 Complexity-associated Testing across NPAAC Categories

A breakdown of the numbers of general, branch, specialised and non-accredited laboratories offering tests within each complexity-related category is provided below (Table 17).

Table 17: Genetic/ Genomic test complexity-associated groups by laboratory NPAAC category (constitutional)

Test groups	Constitutional/ Cancer	No. of Labs	Laboratory NPAAC Category *(number offering each test category)*			
			General	Branch	Specialised	Not Applicable*
Targeted: predefined variant(s) (molecular)	Constitutional	37	22	1	13	1
	Cancer	15	10	-	4	1
Targeted: predefined variant(s) (FISH)	Constitutional	12	9	1	2	-
	Cancer	10	10	-	-	-
Single gene screening	Constitutional	26	14	1	9	2
	Cancer	3	1	-	1	1
2 - 49 genes	Constitutional	21	15	1	5	-
	Cancer	4	2	-	2	-
50+ genes	Constitutional	10	5	1	2	2
	Cancer	1	-	-	-	1
Chromosome screening (karyotyping)	Constitutional	16	12	1	3	-
	Cancer	3	3	-	-	-
Chromosome screening, higher res. (microarray)	Constitutional	18	11	1	6	-
	Cancer	2	2	-	-	-
Exome	Constitutional	5	3	-	1	1
	Cancer	-	-	-	-	-
Genome	Constitutional	2	1	-	-	1
	Cancer	-	-	-	-	-
Gene expression studies	Constitutional	-	-	-	-	-
	Cancer	3	2	-	-	1

** Laboratories without NATA Accreditation.*

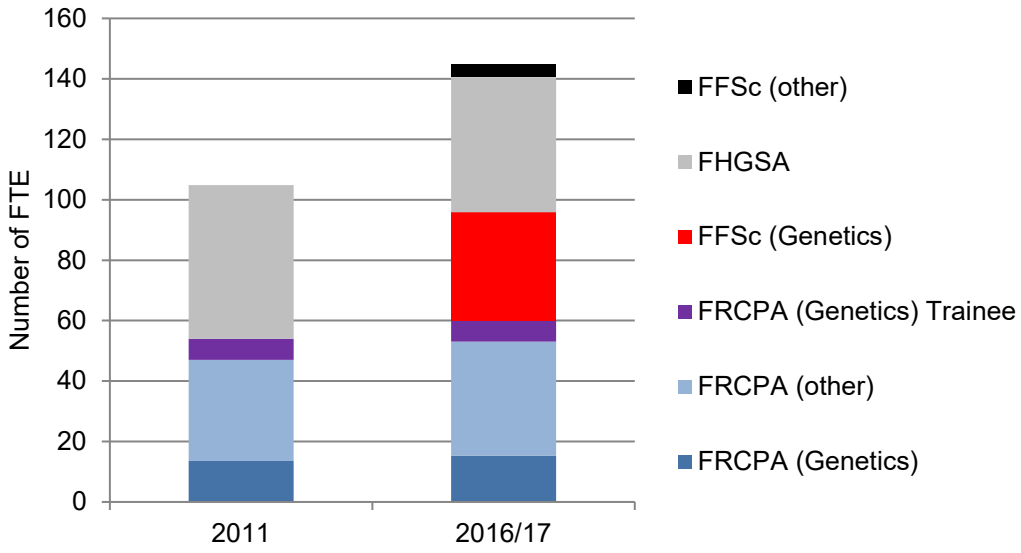
5.3.16 Laboratory Staffing and Supervision

Laboratories were asked to provide details about staffing levels. Information sought included staff professional qualifications and the number of full-time equivalents (FTEs, or portions thereof) of staff time focussed on genetic/ genomic testing. The information provided is summarised below.

5.3.16.1 Workforce Changes

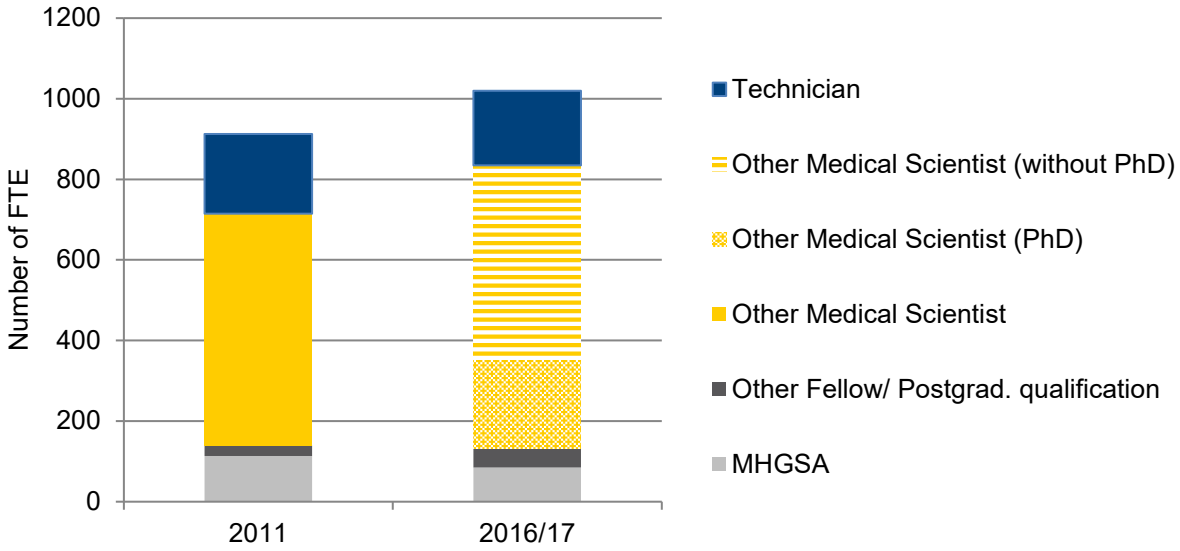
The total number of FTEs identified by this survey was 1287.8. The comparative figure from 2011 was 1010.7. This represents a 27% increase in workforce compared with 2011; however, account should be taken of the wider scope and the inclusion of non-accredited laboratories in the 2016/17 Stocktake. Figures 9 and 10 show the changes in the number of senior medical/ scientific staff and scientific/ technical staff, respectively.

Figure 9: Changes in workforce since 2011 (senior medical/ scientific staff)



The increase in FTE at the senior scientific level (Figure 9) is largely reflective of the establishment of the RCPA Faculty of Science, which was founded in 2009 to provide formal recognition and training of scientists working within the field of pathology. The Faculty has pathways to Fellowship (FFSc) in Genetics or other pathology disciplines by examination or by published research. Additionally, founding Fellows were grandfathered into Fellowship via a strict peer review process.

Figure 10: Changes in workforce since 2011 (scientific/ technical staff)



The 2016/17 survey has also revealed the emergence of staff with a range of other qualifications within the laboratory workforce. Notably, the skills of clinical bioinformaticians (Australia-wide FTE: 21.2) and computer scientists (FTE: 18.2) are being utilised as widespread use of massively parallel sequencing has brought new challenges related to data volumes and complexity. Additionally, genetic counsellors (FTE: 14.3) and clinical geneticists (FTE: 6.5) are now working in several laboratories, with roles including client liaison/ counselling, case coordination, and acquisition of detailed clinical or family history information for case-specific interpretation of results.

5.3.16.2 Workforce Distribution

A breakdown of the distribution of FTEs across states and territories has been completed. This information is presented in Table 18, with comparative data from 2011 shown in parentheses, where available.

Table 18: Staff employed by laboratories offering genetic/ genomic testing, by state/ territory

Staff	FTE by State in 2016/17 (Data from 2011 are in parentheses)*							
	ACT	NSW	QLD	SA	TAS	VIC	WA	Total
FRCPA (Genetics)	0.2	6.3 (3.8)	4.5 (4.2)	1.6 (2.0)	0.0 (0.0)	0.7 (0.1)	2.0 (3.4)	**15.3 (13.5)**
FRCPA (other)	0.5	11.2 (5.2)	8.2 (10.6)	0.6 (1.0)	0.2 (0.0)	6.7 (3.7)	10.3 (13.0)	**37.7 (33.5)**
FFSc (Genetics)	0.6	11.6	1.0	7.0	0.0	10.6	5.0	**35.8**
FFSc (other)	0.0	0.3	1.0	1.0	0.0	0.0	2.0	**4.3**
FRCPA (Genetics) Trainee	0.0	3.0	1.0	1.0	0.0	0.0	2.0	**7.0**
FHGSA	0.0	9.1 (18.2)	8.0 (8.5)	2.0 (3.0)	1.0 (0.0)	19.6 (16.2)	5.0 (5.0)	**44.7 (50.9)**
MHGSA	3	19.5 (24.8)	30.9 (24.8)	1.0 (17.0)	0.0 (2.0)	28.1 (25.6)	2.0 (16.0)	**84.5 (113.8)**
Other Medical Scientist	9.8	201.2 (160.9)	194.6 (143.2)	50.0 (62.1)	4.5 (4.0)	166.6 (133.9)	75.3 (70.4)	**702.0 (574.5)**
Other Fellow	0.0	11 (3.1)	9.3 (6.0)	15.0 (7.0)	0.6 (0.0)	12.0 (4.0)	0.0 (6.0)	**47.9 (26.1)**
Clinical Bioinformatician	0.2	8.7	0.0	3.0	0.0	8.3	1.0	**21.2**
Informatician/ IT/ Computer Scientist	2.1	8.1	0.0	0.0	0.0	6.0	2.0	**18.2**
Technician	6.5	29.0 (22.7)	20.6 (29.3)	27.5 (82.3)	2.5 (3.2)	75.6 (38.0)	23.4 (23.0)	**185.1 (198.5)**
Clinical Geneticist	0.0	4.3	0.0	0.2	0.0	2.0	0.0	**6.5**
Genetic Counsellor	0.0	11.1	0.0	0.0	0.0	3.2	0.0	**14.3**
Other Medical Staff	0.4	5.4	3.0	0.2	0.0	4.0	5.3	**18.3**
Clerical Officer	1.0	9.43	1.4	7.8	0.0	21	4.41	**45**
Total FTE	**24.3**	**349.2 (238.6)**	**283.5 (230.2)**	**117.9 (174.4)**	**8.8 (9.2)**	**364.4 (221.5)**	**139.7 (136.8)**	**1287.8 (1010.7)**

**No equivalent data were collected in 2006 for comparison.*

5.3.16.3 Professional Qualifications of Supervising Staff

For each of the major genetic/ genomic testing categories, service laboratories were grouped according to the highest levels of genetic/ genomic laboratory service-related professional credentialing among the medical and scientific staff within each laboratory, as well as the absence of medical supervision (Table 19).

Medical staff category groups were FRCPA (Genetics); FRCPA (Other Disciplines); Medical Practitioner-Lead (non-FRCPA), and No Medical Supervision. Scientific staff group categories were FFSc (Genetics) or FHGSA; FFSc (Other Disciplines); PhD, and other (None of the above).

Among the laboratories that provided details about staffing, one quarter were supervised by both medical and scientific staff with a qualification indicating professional competency in laboratory genetics/ genomics. A further 15% (12 laboratories) had medical staff credentialed with FRCPA (Genetics).

Thirty-eight percent (31 laboratories) were supervised by medical staff with FRCPA credentialing in disciplines other than genetics. Among these 31 laboratories, 20 (65%) were staffed with scientists with qualifications indicating professional credentialing in genetics.

Four laboratories were supervised by medical practitioners without an FRCPA qualification. Of these, two were staffed with at least one PhD scientist and two were staffed by scientists, none of whom had qualifications indicating professional credentialing in genetics or a PhD. Thirteen laboratories did not have medical staff, however eight of these had genetically-credentialed scientists.

When considering the major laboratory subtypes (biochemical genetics, newborn bloodspot screening, constitutional- and cancer-genetics/ genomics) the numbers in each of the various categories became very much smaller. Despite this, there were some notable observations, including six laboratories providing constitutional genomics testing services without access to either a genetically credentialed scientist or a pathologist of any kind. Among the laboratories offering cancer genetic/ genomic testing, three did not have either a genetically-credentialed scientist or a medical practitioner of any kind.

Table 19: Professional qualifications of supervising laboratory staff

Staff (Medical & Scientific)	Professional Qualifications	Supervising Professional Qualifications (No. of each laboratory type led by staff with the listed qualifications)				Total
		Biochemical Genetics	Newborn bloodspot screening	Genetics / genomics (constitutional)	Genetics / genomics (cancer)	
Medical	FRCPA (genetics)	2	1	9	9	**21**
Scientific	FFSc (genetics) or FHGSA					
Medical	FRCPA (genetics)	1	1	-	-	**2**
Scientific	FFSc (other)					
Medical	FRCPA (genetics)	1	-	2	2	**5**
Scientific	PhD					
Medical	FRCPA (genetics)	-	-	3	2	**5**
Scientific	None of the above					
Medical	FRCPA (other)	2 *(1xH; 1xCP)*	3	9 *(3xAP/H; 2xH; 3xCP, 1xGP)*	6 *(2xAP/H; 2xAP; 1xCP, 1xGP)*	**20**
Scientific	FFSc (genetics) or FHGSA					
Medical	FRCPA (other)	-	-	5 *(1xAP/H; 2xH; 1xI; 1xM)*	4 *(1xAP/H; 2xAP; 1xI)*	**9**
Scientific	PhD					
Medical	FRCPA (other)	-	-	-	2 *(1xAP; 1xH)*	**2**
Scientific	None of the above					
Medical	Medical Practitioner-led (non-FRCPA)	-	-	2	-	**2**
Scientific	PhD					
Medical	Medical Practitioner-led (non-FRCPA)	-	-	2	-	**2**
Scientific	None of the above					
Medical	No medical supervision	1	-	4	3	**8**
Scientific	FFSc (genetics) or FHGSA					
Medical	No medical supervision	-	-	2	2	**4**
Scientific	PhD					
Medical	No medical supervision	-	-	-	1	**1**
Scientific	None of the above					
Total no. of laboratories		**7**	**5**	**38**	**31**	**81**

AP – Anatomical Pathology, H – Haematology, CP – Chemical Pathology, I – Immunology, GP – General Pathology, M – Medical Specialist (non-FRCPA)

5.3.16.4 Professional Qualifications of Supervising Staff and Test Complexity

As described in section 5.3.13.2, genetic/ genomic tests for constitutional disorders or cancer can be categorised into groups that reflect, to some extent, differing levels of technical or interpretive complexity.

The expected standard of care associated with genetic/ genomic testing service provision is that test results are both accurate and accompanied with a clinically-balanced interpretative commentary that may provide direction for clinical decisions regarding medical/ surgical interventions or the reproductive choices of families.

From the viewpoint of public safety, laboratories offering medical genomic testing require a combination of scientific and medical expertise to ensure both valid test results and appropriately formulated interpretive remarks. The importance of the later is increasing with the growing detection of medically significant genomic variants in large sequencing panels or by untargeted methodologies, including microarray, whole exome and whole genome sequencing.

Survey returns offered opportunities to assess the relationship between the diversity of genetic/ genomic tests offered by laboratories and the professional qualifications of their medical and scientific supervising staff. Laboratories were categorised into groups defined by the highest levels of professional qualification obtained by supervising staff, with a specific focus on qualifications demonstrating professional competency in genetic/ genomic testing, as well as the generic competencies required for clinical laboratory service provision.

The group categories were as follows:

1. FRCPA (Genetics), FFSc (Genetics), or both;
2. FHGSA (Genetics);
3. FRCPA (non-Genetics), FFSc (non-Genetics), or both;
4. Medical Practitioner-led (non-FRCPA Pathologist);
5. Scientist-led (PhD), and
6. Scientist-led (other).

For each test complexity-related group, the proportions of all tests performed in each qualification-defined category are summarised in Tables 20-22. Where applicable, additional breakdowns of sub-groups within each of the major group categories are included within the tables.

Table 20: Percentage of tests performed under supervision of staff with relevant professional qualifications (constitutional)

Test categories	Total number of tests	Supervising Professional Qualifications (% of constitutional genetic/ genomic testing performed under the listed supervision categories)					
		FRCPA (Genetics), FFSc (Genetics), or both	FHGSA (Genetics)	FRCPA (non-Genetics), FFSc (non-Genetics), or both	Medical Practitioner-led (non-FRCPA Pathologist)	Scientist-led (PhD)	Scientist-led (other)
Targeted testing for predefined genomic variants (molecular)	414320	85% (Both 37%; FRCPA 38%; FFSc 11%)	6%	6% (Both <1%; FRCPA 6%; FFSc 0%)	2%	<1%	-
Targeted testing for predefined genomic variants (FISH)	4961	75% (Both 58%; FRCPA 13%; FFSc 5%)	25%	-	-	-	-
Targeted screening for undefined variants in a single gene	6339	57% (Both 44%; FRCPA 6%; FFSc 7%)	35%	8% (Both 0%; FRCPA 8%; FFSc 0%)	1%	-	-
Targeted screening for undefined variants in 2-49 genes	13899	50% (Both 30%; FRCPA 4%; FFSc 17%)	13%	37% (Both 0%; FRCPA 37%; FFSc 0%)	<1%	-	-
Targeted screening for undefined variants in 50 or more genes	2883	94% (Both 44%; FRCPA 2%; FFSc 49%)	6%	-	-	-	-
Untargeted screening of all chromosomes (karyotyping)	55613	64% (Both 29%; FRCPA 33%; FFSc 1%)	36%	-	-	-	-
Untargeted higher-res. screening of chromosomes (microarray)	38358	79% (Both 58%; FRCPA 10%; FFSc 11%)	9%	1% (Both 0%; FRCPA 1%; FFSc 0%)	-	11%	-
Untargeted screening of whole exome	342	13% (Both 13%; FRCPA 0%; FFSc 0%)	-	-	13%	73%	-
Untargeted screening of whole genome	323	100% (Both 100%; FRCPA 0%; FFSc 0%)	-	-	-	-	-

Tests have been assigned to one of the above supervisory categories based on the professional qualifications of the staff at the testing laboratory. The six broad supervisory categories (columns) have been treated as mutually exclusive; where multiple qualifications apply, tests have been assigned to the furthest left applicable column. Tests performed in research laboratories have been excluded from this analysis.

Table 21: Percentage of tests performed under supervision of staff with relevant professional qualifications (cancer)

Test categories	Total number of tests	Supervising Professional Qualifications (% of cancer genetic / genomic testing performed under the listed supervision categories)					
		FRCPA (Genetics), FFSc (Genetics), or both	FHGSA (Genetics)	FRCPA (non-Genetics), FFSc (non-Genetics), or both	Medical Practitioner-led (non-FRCPA Pathologist)	Scientist-led (PhD)	Scientist-led (other)
Targeted testing for predefined genomic variants (molecular)	64132	75% (Both 32%; FRCPA 29%; FFSc 14%)	4%	13% (FRCPA 13%; FFSc 0%)	-	8%	-
Targeted testing for predefined genomic variants (FISH)	16509	83% (Both 33%; FRCPA 27%; FFSc 23%)	8%	2% (FRCPA 2%; FFSc 0%)	-	1%	6%
Targeted screening for undefined variants in a single gene	75	95% (Both 0%; FRCPA 0%; FFSc 95%)	5%	-	-	-	-
Targeted screening for undefined variants in 2-49 genes	8859	44% (Both 6%; FRCPA 4%; FFSc 34%)	-	56% (FRCPA 56%; FFSc 0%)	-	-	-
Targeted screening for undefined variants in 50 or more genes	2101	100% (Both 0%; FRCPA 12%; FFSc 88%)	-	-	-	-	-
Untargeted screening of all chromosomes (karyotyping)	20102	81% (Both 32%; FRCPA 45%; FFSc 4%)	3%	-	-	16%	-
Untargeted higher-res. screening of chromosomes (microarray)	1436	98% (Both 54%; FRCPA 0%; FFSc 44%)	-	2%	-	-	-
Gene expression studies	131	100% (Both 0%; FRCPA 0%; FFSc 100%)	-	-	-	-	-

Tests have been assigned to one of the above supervisory categories based on the professional qualifications of the staff at the testing laboratory. The six broad supervisory categories (columns) have been treated as mutually exclusive; where multiple qualifications apply, tests have been assigned to the furthest left applicable column. Tests performed in research laboratories have been excluded from this analysis.

Table 22: Percentage of tests performed under supervision of staff with relevant professional qualifications (biochemical, excluding newborn bloodspot screening and maternal serum screening)

Total number of tests	Supervising Professional Qualifications (% of biochemical genetic testing performed under the listed supervision categories)					
	FRCPA (Genetics), FFSc (Genetics), or both	FGHSA (Genetics)	FRCPA (non-Genetics), FFSc (non-Genetics), or both	Medical Practitioner-led (non-FRCPA Pathologist)	Scientist-led (PhD)	Scientist-led (other)
67284	100% (Both 18%; FRCPA 27%; FFSc 55%)	0%	0%	0%	0%	0%

Tests have been assigned to one of the above supervisory categories based on the professional qualifications of the staff at the testing laboratory. The six broad supervisory categories (columns) have been treated as mutually exclusive; where multiple qualifications apply, tests have been assigned to the furthest left applicable column.

5.3.16.5 Professional Qualifications of Supervising Staff and Test Methods

Survey returns also offered insights into the relationship between the range of methods used by laboratories and the professional qualifications of supervising medical and scientific staff.

For each test method used within the various testing categories, participating laboratories were grouped according to the highest professional qualification held by medically-qualified or scientific supervising staff (Tables 23 and 24, respectively).

Table 23: Medical supervision at service laboratories, by test method

Test scope category / Test method	Medical supervision (No. of laboratories using test method)				Total no. of laboratories using test method
	FRCPA (medical genomics)	FRCPA (other)	Non-FRCPA	Nil	
Targeted testing for presence/ absence of predefined genomic variation					**Totals**
NAAT (end-point)	12	16	1	8	**37**
NAAT (quantitative, excl. ddPCR)	8	12	1	6	**27**
FISH	8	7	-	6	**21**
Sanger sequencing	6	4	-	5	**15**
MLPA	6	6	1	2	**15**
Massively parallel sequencing	5	6	1	4	**16**
Single nucleotide primer extension	4	2		2	**8**
Microarray	2	3	1	2	**8**
ddPCR	1	4	-	-	**5**
MALDI-TOF	1	3	-	-	**4**
Sanger sequencing & MLPA	4	1	-	-	**5**
Southern blot	1	1	1	-	**3**
NAAT (end-point) & Southern blot	1	1	-	-	**2**
Targeted screening for undefined variants in 1 or 2 genes					
Sanger sequencing	6	4	2	3	**15**
Sanger sequencing & MLPA	6	2	-	3	**11**
Massively parallel sequencing	3	3	-	2	**8**
MPS & MLPA	4	1	-	1	**6**
Targeted screening for undefined variants in 3 – 50 genes					
Massively parallel sequencing	6	7	-	4	**17**
MPS & MLPA	4	-	-	3	**7**
Sanger sequencing	3	-	1	1	**5**
Sanger sequencing & MLPA	2	-	1	-	**3**
Targeted screening for undefined variants in more than 50 specified genes					
Massively parallel sequencing	5	3	-	2	**10**
Untargeted screening of all chromosomes (karyotyping)					
Microscopy	10	5	-	3	**18**
Untargeted higher-resolution screening of all chromosomes					
Microarray	7	8	1	4	**20**
Untargeted screening of whole exome					
Massively parallel sequencing	2	-	1	1	**4**
Untargeted screening of whole genome					
Massively parallel sequencing	1	-	-	-	**1**
Gene expression studies					
NAAT (quantitative, excl. ddPCR)	-	1	-	1	**2**

Abbreviations: ddPCR Droplet digital PCR; FISH Fluorescent in situ hybridisation; MALDI-TOF Matrix-assisted laser

desorption/ ionisation time-of-flight mass spectrometry; MLPA Multiplex ligation-dependent probe amplification; MPS Massively parallel sequencing; NAAT Nucleic acid amplification test

Table 24: Scientific supervision at service laboratories, by test method

Test scope category / Test method	Scientific supervision (No. of laboratories using test method)					Total no. of laboratories using test method
	FFSc; FHGSA (genomics) (examn.)	FFSc (genomics) (founding, research)	FFSc (other)	PhD	Other	
Targeted testing for presence/ absence of predefined genomic variation						**Totals**
NAAT (end-point)	14	7	-	12	4	**37**
NAAT (quantitative, excl. ddPCR)	10	5	-	10	2	**27**
FISH	14	3	-	1	3	**21**
Sanger sequencing	5	5	1	3	1	**15**
MLPA	7	4	1	2	1	**15**
Massively parallel sequencing	6	4	-	5	1	**16**
Single nucleotide primer extension	4	1	-	3	1	**9**
Microarray	1	2	-	5	-	**8**
ddPCR	1	1	-	1	2	**5**
MALDI-TOF	1	2	-	-	1	**4**
Sanger sequencing & MLPA	3	2	-	-	-	**5**
Southern blot	2	-	-	-	1	**3**
NAAT (end-point) & Southern blot	1	1	-	-	-	**2**
Targeted screening for undefined variants in 1 or 2 genes						
Sanger sequencing	6	3	-	5	1	**15**
Sanger sequencing & MLPA	6	4	-		1	**11**
Massively parallel sequencing	3	2	-	2	1	**8**
MPS & MLPA	3	2	-	-	1	**6**
Targeted screening for undefined variants in 3 – 50 genes						
Massively parallel sequencing	6	6	-	3	2	**17**
MPS & MLPA	6	1	-	-		**7**
Sanger sequencing	2	2	-	-	1	**5**
Sanger sequencing & MLPA	1	1	-	-	1	**3**
Targeted screening for undefined variants in more than 50 specified genes						
Massively parallel sequencing	4	3	1	-	2	**10**
Untargeted screening of all chromosomes (karyotyping)						
Microscopy	13	3	-	2	1	**19**
Untargeted higher-resolution screening of all chromosomes						
Microarray	12	3	-	5	-	**20**
Untargeted screening of whole exome						
Massively parallel sequencing	1	1	-	1	1	**4**
Untargeted screening of whole genome						
Massively parallel sequencing	-	1	-	-	-	**1**
Gene expression studies						
NAAT (quantitative, excl. ddPCR)	1	1	-	-	-	**2**

Abbreviations: ddPCR Droplet digital PCR; FISH Fluorescent in situ hybridisation; MALDI-TOF Matrix-assisted laser desorption/ ionisation time-of-flight mass spectrometry; MLPA Multiplex ligation-dependent probe amplification; MPS Massively parallel sequencing; NAAT Nucleic acid amplification test.

5.3.17 Sample Registration, Tracking and Report Storage

Laboratories were asked to indicate how information pertaining to request and sample registration, workflow and sample tracking, and issued reports were stored (Tables 25–27).

The majority of Biochemical Genetics and Chemical Pathology laboratories used laboratory information management systems (LIMS) for all three processes. There was considerable variation in the types of systems used among other laboratories; although LIMS were also most commonly used for all three processes. Other sample registration, tracking and report storage systems included local electronic records or databases, either laboratory-based or hospital servers; a combination of a local electronic record/ database and LIMS; a local electronic record or database stored on a laboratory hard drive, or laboratory workbooks.

In the 2016/17 financial year, more than half of all service laboratories used LIMS for test request/ sample registration (69.1%) and report storage (57.6%). A lower proportion retained workflow and sample tracking details in the LIMS (44.2%) and 17% of all laboratories were still using either laboratory hard drives or workbooks for these processes. As these details were not sought in the earlier two surveys, it is not possible to comment on the rate of upgrading of information management systems within genetic/ genomic testing sectors.

Table 25: Test request and sample registration

Registration	Number of laboratories			Percent
	Service	Research	Total	
LIMS	27	1	28	48.4
Local electronic record/ database (laboratory/ hospital server)	9	5	14	24.1
Local system and LIMS	9	3	12	20.7
Local electronic record/ database (laboratory hard drive)	1	1	2	3.4
Laboratory workbooks	0	2	2	3.4
Total	46	12	58	100

Table 26: Test workflow and sample tracking

Workflow/Sample Tracking	Number of laboratories			Percent
	Service	Research	Total	
LIMS	16	1	17	28.8
Local electronic record/ database (laboratory/ hospital server)	13	4	17	28.8
Local system and LIMS	12	3	15	25.4
Local electronic record/ database (laboratory hard drive)	4	1	5	8.5
Laboratory workbooks	2	3	5	8.5
Total	47	12	59	100

Table 27: Test report storage

Storage of Reports	Number of laboratories			Percent
	Service	Research	Total	
LIMS	31	3	34	57.6
Local electronic record/ database (laboratory/ hospital server)	12	7	19	32.2
Local electronic record/ database (laboratory hard drive)	3	0	3	5.1
Hardcopy	1	2	3	5.1
Total	47	12	59	100

5.3.18 Genomic Data Storage

Laboratories were asked to provide information about the infrastructure used for data storage, as well as policies and practices regarding local storage of details about locally identified curated genomic variants. Laboratories were also asked to describe whether details of their curated variants were submitted to international databases, such as ClinVar or DECIPHER, which are widely used by Australian genetic/ genomic laboratories to aid variant clinical classification.

Genomic data generated from patient samples were stored on a wide range of platforms, of which hospital servers (29%), local laboratory servers (21%), and “multiple storage systems” (22%) were the most frequent (Table 28).

Table 28: Data storage infrastructure

Infrastructure	Number of laboratories			Percent
	Service	Research	Total	
Hospital server	17	3	20	29.4
Local server in lab	8	6	14	20.6
Cloud storage	4	0	4	5.9
External data warehouse	2	0	2	2.9
Local hard drive	0	1	1	1.5
Local portable storage device(s)	1	0	1	1.5
Multiple * (listed below)	12	3	15	22.0
Other ** (listed below)	11	0	11	16.2
Total	55	13	68	100

*** Multiple**

- Cloud storage: DNANexus; Centralised network storage; local NAS drive
- External data warehouse server; Local server
- External data warehouse; hospital server, Laboratory server
- Cloud storage; Hospital IT service
- Pathology LIMS; Local laboratory database
- Hospital server; Local laboratory server
- Hospital server; Portable hard drive
- University secured servers/tape; Local hard drive
- Clinic server, Portable hard drives
- Network, External hard drives, DVD
- Cloud storage; Local laboratory server (research)
- University server; Hard copies (research)

**** Other**

- Institute server with off-site backup (full disaster recovery)
- International security server
- In-house network solution
- Business on-site and off-site servers
- Shared server within the institution

Laboratories were also asked to indicate whether they were satisfied with their data storage facilities. If dissatisfied, laboratories were asked to list their concerns and outline potential solutions, as well as the factors required to implement these improvements. Responses are summarised in Tables 29 and 30.

Approximately two thirds of service laboratories and most research laboratories were satisfied with their current data storage infrastructure. Concerns that were raised by the remaining one third of laboratories mainly related to “future proofing” and insufficiency of backed-up storage space.

Table 29: Satisfaction with data storage infrastructure

Satisfied	Number of laboratories			Percent
	Service	Research	Total	
Yes	35	11	46	69.6
No	19	1	20	30.3
Total	54	12	66	100

Table 30: Issues and potential solutions regarding data storage infrastructure

Sector	Issue(s)	Solution	Solution Requirement
Service	Insufficient storage infrastructure	Cloud storage	Finance, implementation of new LIS
	Slow implementation; Not "future proofed"	Cloud storage	change in practise, time and resources
	Insufficient backed-up storage space.	LIMS appropriate for genetic/ genomic testing	Ability to purchase or construct an appropriate LIMS and data storage facility
	Not "future proofed"	Cloud storage	Finance
	Not "future proofed"	Cloud storage	Support and resources from Local and Health IT
	Portable hard drive storage; insecure and cumbersome	More data storage on hospital server	Business case for increased data storage capacity requires approval
	Limited access to Pathology LIMS has necessitated numerous "workarounds"	Full laboratory access to Pathology LIMS	Agreement between different business units
	Differing data storage systems across public sector sites/labs	Centralised data storage, leveraging cloud storage	Enabling regulatory framework; finance, stakeholder engagement and consensus
	Insufficient storage; Not "future proofed"	Off-site storage	Funds
	Insufficient local storage infrastructure	Cloud storage or improved local infrastructure	Support from local IT
	Insufficient backed-up storage space	Access to GovNext, a state government storage warehouse	Approval from several government departments; selection of GovNext service provider
Research	Capacity and computing power for analysis of data; data security	Scalable cloud and server resources	Secure, scalable and configurable cloud storage resource

It is standard practice to compare genomic variations identified during clinical testing with variants recorded in a range of databases and within scientific literature. Comparison with both local and international databases is an essential step in the clinical interpretation of many genomic variants.

Laboratories were asked to indicate if details of locally-identified variants were retained in a searchable local database for future reference. Approximately one third of laboratories performing genetic/ genomic testing did not retain any variants in a searchable database (Table 31).

Table 31: Retention of locally-identified variants in searchable local databases

Local variants	Number of laboratories			Percent
	Service	Research	Total	
Yes – all variants	23	6	29	42.6
Yes – some variants	12	5	17	25.0
No	20	2	22	32.4
Total	55	13	68	100

Laboratories storing information about identified variants were also asked to indicate whether local databases were developed in-house or sourced commercially. More than half used in-house databases (Table 32).

Table 32: Nature of local variant databases

Local database type	Number of laboratories			Percent
	Service	Research	Total	
In house	17	9	26	56.5
Commercial	5	0	5	10.9
Both	14	1	15	32.6
Total	36	10	46	100

5.3.19 Contribution to International Databases

Globally, laboratories routinely refer to international variant databases when determining the clinical significance of genomic variants identified in patient samples. Through sharing details of curated variants, a broader repository of data is generated, which facilitates the accurate interpretation of genomic results and ultimately improves patient care.

Laboratories were asked to indicate if details of locally curated variants were submitted to any of the international genomic/ cytogenomic databases typically used by service laboratories for variant clinical classification. Less than half of all laboratories offering sequencing tests, where variants of uncertain clinical significance may be found, reported submitting details of their identified variants to relevant international databases. Among these, only one laboratory reported submitting details of all identified variants to relevant external databases during the survey period (Table 33).

The comments provided by laboratories that did submit details of variants to international genomic/ cytogenomic databases are provided below, as well as a list of the recipient repositories (Table 34).

Table 33: Submission of variant details to external databases

Variant details submitted to external databases	Number of laboratories			Percent
	Service	Research	Total	
No	41	9	50	73.5
Yes – some variants	13	4	17	25.0
Yes – all variants	1	0	1	1.5
Total	55	13	68	100

Laboratories not contributing details of locally curated variants were asked to list the factor(s) preventing submission. The comments offered are listed below:

- Manual submission processes (insufficient resources)
- Insufficient bioinformatics resources
- Staff time constraints
- Inability to provide associated clinical details
- Perception that variants must be published prior to submission to databases
- Indecision regarding databases to which submissions are made
- Concerns about confidentiality
- In vitro functional characterisation required
- Ongoing discussions with Human Variome Project about formatting and storage requirements (research)

Table 34: Types of variants submitted and the databases to which they are submitted

Sector	Variants submitted to external databases	External database name(s)
Service	Only pathogenic, likely pathogenic & variants of uncertain significance submitted	ClinVar
	Somatic variants	ClinVar
	Novel variants	ClinVar
	Curated variants (uncertain (class 3), likely pathogenic (class 4) and pathogenic (class 5))	ClinVar, LOVD
	Novel HLA alleles	IMGT
	Comment from a state public sector group of laboratories: Variant submission varies across sites; issue being addressed in current projects	
Research	Novel alleles after proof of causation	OMIM
	Variants assessed as being pathogenic or possibly pathogenic	HGMD; LOVD

5.3.20 Reporting Times

Laboratories were asked to provide details about reporting turnaround times from the date of receipt of the sample and request (median and 90th centiles, in calendar days). Survey returns were summarised for clinical referral categories and subcategories (Table 35), as well as test complexity-related categories for both constitutional- and cancer-related testing (Table 36).

Table 35: Reporting times (calendar days) by clinical referral category

Clinical referral categories			Reporting Times			
Subcategories	Total no. test targets/ types offered across all labs.	No. instances where reporting time provided	Median	Range	90th Centile	Range
Diagnostic						
Symptomatic patient (constitutional)	617	485	28	1-237	45	1-377
Symptomatic patient (cancer)	365	261	9	1-96	14	3-100
Family segregation analysis (to assist variant classification)	45	23	24	10-127	24	10-231
Familial cascade testing of a known pathogenic variant	145	82	22	7-136	32	9-167
Carrier testing (autosomal and X-linked recessive disorders)	65	56	19	7-104	30	10-198
Therapy selection/ monitoring						
Tumour sample genotyping	95	70	7	1-30	10	2-110
Minimal residual disease/ transplant monitoring	21	21	9	2-21	10	2-100
Pharmacogenomic testing (constitutional)	19	18	5	3-23	5	7-41
Prenatal						
Maternal blood (fetal aneuploidy screening)	6	6	5	2-10	9	5-12
Pre-implantation genetic testing						
Aneuploidy screening	12	8	10	3-23	12	3-23
High risk monogenic disease testing	5	4	13	8-29	17	10-29

Table 36: Reporting times (calendar days) for diagnostic tests (constitutional and cancer)

Test categories	Service Category	Reporting Times			
		Median	Range	90th Centile	Range
Targeted testing for predefined genomic variants (molecular)	Constitutional	11	1-106	21	3-190
	Cancer	9	1-54	14	3-100
Targeted testing for predefined genomic variants (FISH)	Constitutional	5	1-9	8	1-45
	Cancer	9	1-56	13	3-70
Targeted screening for undefined variants in a single gene	Constitutional	42	5-201	57	7-300
	Cancer	45	-	100	-
Targeted screening for undefined variants in fewer than 50 genes	Constitutional	49	1-217	70	3*-314
	Cancer	**	4-12	**	7-14
Targeted screening for undefined variants in 50 or more genes	Constitutional	60	14-119	96	21-204
	Cancer	42	12-96	100	14-100
Untargeted screening of all chromosomes (karyotyping)	Constitutional	17	7-49	22	8-63
	Cancer	14	6-35	21	8-62
Untargeted higher-res. screening of chromosomes (microarray)	Constitutional	19	8-63	25	12-107
	Cancer	18	7-33	32	10-55
Exome	Constitutional	72	50-119	120	72-164
	Cancer	-	-	-	-
Genome	Constitutional	102	-	139	-
	Cancer	-	-	-	-

** HLA testing. The most rapid end of the range for diagnostic testing for constitutional disorders was 14 days.*
*** Data from two laboratories only*

5.3.21 Funding

Laboratories were asked to indicate the source of funding for tests on samples originating within the same state/ territory and also for tests performed on samples received from other states/ territories. As described in Section 5.3.14, the source of funding was not provided for 18% of constitutional tests, 24% of cancer tests and 4% of biochemical diagnostic tests (excluding newborn bloodspot screening and maternal serum screening). Funding data are summarised below (Figures 11–14, Tables 37 & 38).

Figure 11: Sources of funding for within-state and interstate samples (constitutional)

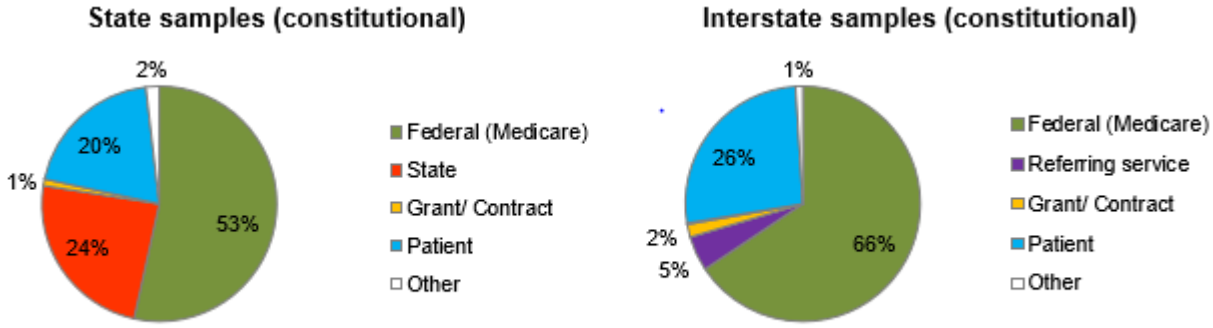


Figure 12: Sources of funding for within-state and interstate samples (cancer)

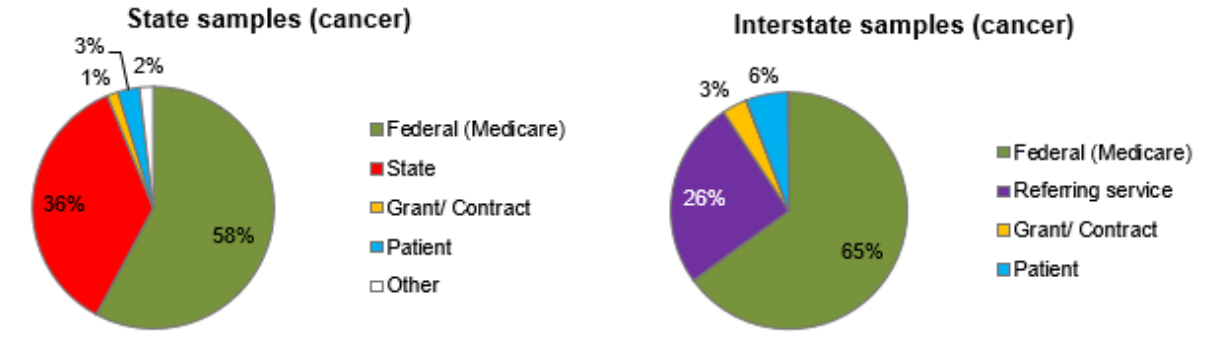


Figure 13: Sources of funding for biochemical diagnostic samples (excluding MSS and NBS)

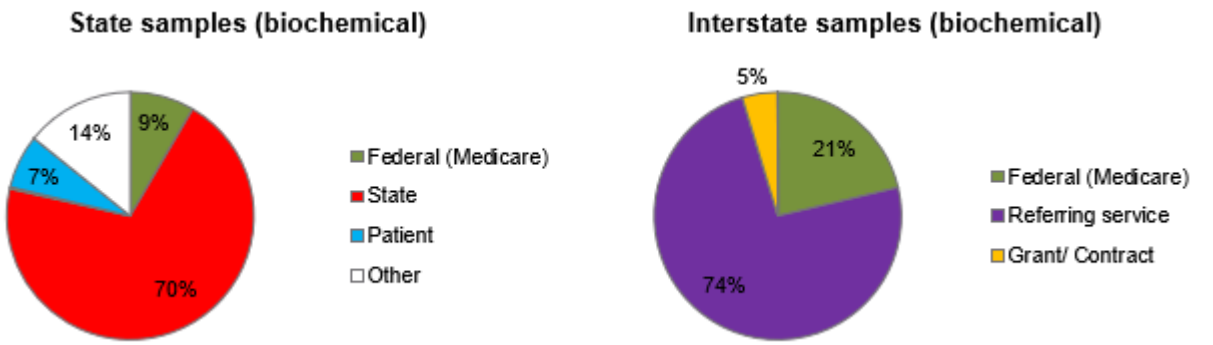
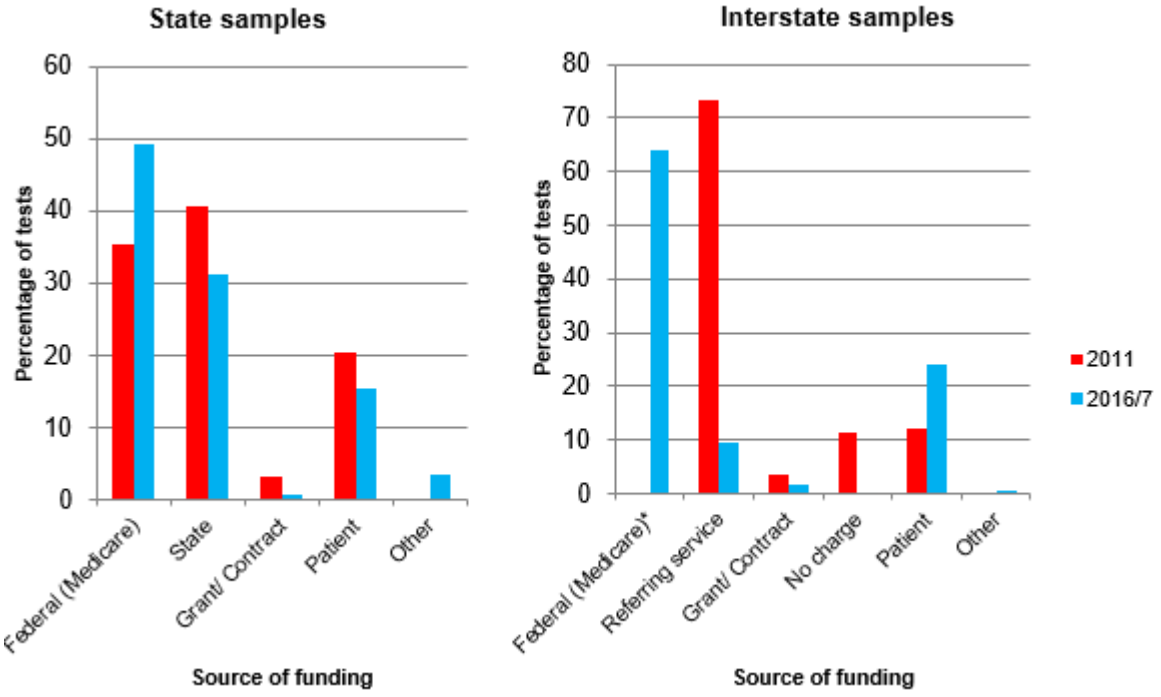


Figure 14: Sources of funding for constitutional, cancer and biochemical tests (2011 *vs.* 2016/17)



Note: Data are inclusive of constitutional, cancer and biochemical diagnostic tests. HLA comprehensive sequencing, newborn bloodspot screening and maternal serum screening have been excluded to allow comparison with 2011

** Data on Medicare funding for interstate samples not provided in 2011.*

The 2016/17 survey data revealed that funding arrangements for genetic/ genomic tests have changed substantially. For within-state tests, federal funding (Medicare) covered almost half (49%) of tests in 2016/17, compared with approximately 35% in 2011. There have been corresponding falls in the proportion of tests funded by most other sources. The change in the proportion of tests covered by federal funding was largely reflective of an increase in requests for tests with longstanding MBS item numbers, rather than the result of addition of new MBS items over the last 5 ½ years.

Survey data revealed several notable differences in funding arrangements for samples that had been transferred across state borders for testing compared with tests performed locally. Approximately two thirds of interstate constitutional tests (66%) were federally funded, 99% of which were performed in private laboratories. A similar proportion of interstate cancer tests (65%) were federally funded and 89% of these were performed in private laboratories. Details on federal funding did not appear to have been captured for interstate samples in the 2011 survey. Review of the 2011 distribution of funding sources for interstate samples, however, raises the possibility that Medicare funding contributed to a substantial proportion of tests listed then as having been funded by referring services.

The proportion of interstate tests paid for by patients has doubled since 2011 to approximately a quarter of these tests. This is largely reflective of the growing uptake of non-invasive prenatal screening for chromosomal aneuploidies which, during the 2016/17 financial year, was offered by only a few laboratories and accounted for 65% of patient-funded interstate constitutional tests. Pre-implantation aneuploidy screening accounted for a further 13% of interstate constitutional tests.

Most biochemical diagnostic tests are funded by the States (Figure 13). As observed in the 2011 survey, biochemical genetic testing continues to attract negligible federal funding.

Tables 37 and 38 provide a breakdown of the sources of funding for constitutional and cancer tests by state-/ territory-of-origin of the sample. The data summarised within these tables should be considered with the following caveats:

1. Details about the state-/ territory-of-origin of samples were not available for approximately 118,500 tests (16.3%) of samples.
2. The source of funding was not provided for 18% of constitutional tests, 24% of cancer tests and 4% of biochemical diagnostic tests (excluding newborn bloodspot screening and maternal serum screening)

Several notable differences are evident in the funding of genetic/ genomic tests across states/ territories, particularly in the proportions of federal-, state- and patient-funded tests. The extent of the differences suggests that the above caveats may apply and care must be taken in drawing conclusions from these data. Further comparison can be made against published Medicare statistics. Table 39 lists the Medicare services per capita for high-volume constitutional and cancer tests over the 2016/17 financial year; it also demonstrates notable differences across states/ territories.

Table 37: Funding sources for constitutional tests

Patient location	Percent of total funding							
Funding Source	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Local (within state or territory)								
Federal (Medicare)	58.5	69.3	-	51.4	54.6	78.7	45.0	25.8
State	37.9	12.3	-	34.1	36.8	14.1	20.8	56.3
Grant/ Contract	0	0.4	-	1.0	0	0	0.7	5.5
Patient	3.0	16.9	-	13.2	8.6	7.2	31.7	1.4
Other	0.6	1.1	-	0.5	0	0	1.9	11.1
Total (%)	**100**	**100**	-	**100**	**100**	**100**	**100**	**100**
Interstate								
Federal (Medicare)	64.8	56.9	25.7	71.9	79.5	77.4	60.8	72.6
Referring service	6.2	3.7	70.5	16.0	0.8	10.5	2.6	0.7
Grant/ Contract	0.8	1.4	0.9	0.6	0.6	0.1	5.1	1.0
No charge	2.2	0.0	0.0	0.1	0.0	0.0	0.0	0.0
Patient	25.1	35.8	0.4	11.1	18.9	10.3	31.2	25.7
Other	0.9	2.2	2.4	0.3	0.2	1.7	0.2	0.0
Total (%)	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

Table 38: Funding sources for cancer tests

Patient location	Percent of total funding							
Funding Source	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Local (within state or territory)								
Federal (Medicare)	61.7	68.2	-	55.8	80.2	41.5	41.3	41.7
State	32.8	21.2	-	41.8	18.0	54.3	51.9	54.1
Grant/ Contract	0.0	1.8	-	0.0	0.2	0.0	3.5	0.3
Patient	5.1	5.1	-	2.4	0.5	4.1	1.6	2.7
Other	0.4	3.8	-	0.0	1.1	0.0	1.7	1.3
Total (%)	**100**	**100**	-	**100**	**100**	**100**	**100**	**100**
Interstate								
Federal (Medicare)	21.6	75.4	43.7	32.6	78.3	50.3	72.0	73.5
Referring service	66.3	14.6	46.9	55.5	12.3	47.6	19.8	18.7
Grant/ Contract	3.4	0.9	9.5	11.5	6.4	1.0	2.8	4.1
No charge	0.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Patient	7.9	9.1	0.0	0.0	2.5	1.1	5.2	3.6
Other	0.0	0.0	0.0	0.3	0.5	0.0	0.2	0.1
Total (%)	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

Table 39: Medicare services per capita, by state/ territory (high volume assays)

Item	Description	Services per 100,000 population (MBS data*)								
		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Nation wide
Constitutional										
73317	Detection of C282Y in the *HFE* gene in a patient with consistently elevated TS or SF, or a first degree relative with haemochromatosis or homozygosity for C282Y/ relevant compound heterozygosity	449	261	191	350	261	406	196	159	**257**
73287	The study of the whole of every chromosome by cytogenetic or other techniques, performed on 1 or more of any tissue or fluid except blood	46	53	13	27	47	21	49	53	**45**
73289	The study of the whole of every chromosome by cytogenetic or other techniques, performed on blood	136	223	101	209	106	192	175	240	**198**
73292	Analysis of chromosomes by genome-wide microarray in a person with developmental delay, intellectual disability, autism, or at least two congenital abnormalities	64	76	66	41	67	80	90	23	**66**
73308	Characterisation of the genotype of a patient for Factor V Leiden gene mutation, or detection of the other relevant mutations in the investigation of proven venous thrombosis or pulmonary embolism	159	100	52	86	153	97	89	113	**100**
73311	Characterisation of the genotype of a person who is a first degree relative of a person who has proven to have 1 or more abnormal genotypes under item 73308	18	12	4	26	15	36	11	20	**16**
73300	Detection of a mutation of the *FMR1* gene	43	48	41	24	58	46	59	20	**43**
73320	Detection of HLA-B27 by nucleic acid amplification	317	62	14	249	163	23	81	6	**109**
71147	HLA-B27 typing	111	233	188	263	162	197	179	345	**229**
71151	Tissue typing for HLA-DR, HLA-DP and HLA-DQ Class II antigens - phenotyping or genotyping of 2 or more antigens	116	138	143	144	145	147	246	126	**165**
Cancer										
73287	The study of the whole of every chromosome by cytogenetic or other techniques, performed on 1 or more of any tissue or fluid except blood	46	53	13	27	47	21	49	53	**45**
73290	The study of the whole of each chromosome by cytogenetic or other techniques, performed on blood or bone marrow, in the diagnosis and monitoring of haematological malignancy	78	41	1	87	4	58	2	4	**35**
73314	Characterisation of gene rearrangement or the identification of mutations within a known gene rearrangement, in the diagnosis and monitoring of patients with laboratory evidence of AML, APML, ALL, or CML	55	60	5	103	57	27	54	7	**60**

Item	Description	Services per 100,000 population (MBS data*)							
		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Nation wide
Constitutional										
73315	A test described in item 73314, if rendered by a receiving approved pathology practitioner	14	24	1	5	7	39	7	25	**14**
73325	Characterisation of mutations in *JAK2*, *MPL*, or both genes, in a patient with clinical and laboratory evidence of PV or ET.	43	52	12	81	42	43	45	32	**52**

AML Acute myeloid leukaemia; APML Acute promyelocytic leukaemia; ALL Acute lymphoid leukaemia; CML Chronic myeloid leukaemia; ET Essential thrombocythaemia; PV Polycythaemia vera; TS Transferrin saturation; SF Serum ferritin
**Data obtained from published Medicare statistics [3].*

6. Discussion

In keeping with the two previous surveys, the 2016/17 stocktake of national genetic and genomic testing has yielded many useful insights into the growing scope and increasing clinical demand for genetic/ genomic tests. It has also identified several important challenges facing many of the laboratories providing these services.

6.1 Outcomes

With a laboratory participation rate of 95.4%, the 2016/17 National Stocktake of Genetic and Genomic Testing received valuable and informative data from a broader range of participants, compared to previous surveys. The 2016/17 Stocktake differed from the 2011 Survey, which targeted services provided by NATA accredited laboratories. This most recent survey sought details from all laboratories, including research groups, known to have issued test results to referring doctors. Compared with 39 participating laboratories in 2011, the number of accredited laboratories participating in 2016/17 was 72, representing an 85% increase. Eight additional laboratories without accreditation participated in the 2016/17 survey, seven of which were in the research sector.

A total of 1,181,923 tests were reported. They comprised 660,150 genomic tests (constitutional – 545,029; cancer – 115,121); maternal serum screening (146,719); newborn bloodspot screening (307,770), and biochemical genetic diagnostic tests (67,284).

Just over half of all completed investigations (53.6%) were delivered by the private sector, which was represented by 30% of participating laboratories. The public sector, comprising 51.3% of laboratories, delivered 45.1% of tests. The remaining 1.3% of tests were delivered by laboratories categorised as research (15% of participating laboratories) or Catholic/ schedule 3 (3.8% of laboratories).

6.2 Issues and Limitations

6.2.1 Data Access Restrictions

Although the overall rate of participation was high, most laboratories were unable to provide all details sought by the survey. In many instances, the missing data were relatively minor (e.g. reporting times). However, a small number of laboratories did not provide any information about tests or, alternatively, accreditation status, staffing or laboratory infrastructure. It is to be expected that these missing data will have exerted some influence on the survey findings. However, it became apparent during the analysis that potential major biases arising from data gaps were limited to subsets of results – most especially information about the state-of-origin of patients. This subsequently prevented exploration of questions regarding regional equity of access to testing services.

Echoing the experiences of the 2011 survey, it became evident during the course of this survey that the capacity of many laboratories to provide data was limited by the capabilities currently embedded within their laboratory information management systems – either for prior capture of specific details (for example clinical indications for testing or the specialty categories of referring doctors), or the retrieval of details from archived records, including details about the numbers of assays completed by laboratories for quality control purposes.

A further challenge encountered on this occasion was the reluctance of several commercial laboratories to provide data regarded as commercially sensitive. It is understood that a similar hesitancy was encountered during the 2011 survey, which was then successfully overcome by the Survey Leads. Despite major efforts directed towards addressing the reasons for the reluctance during this most recent survey, most, but not all, of these laboratories remained steadfast in their decisions either not to participate or to withhold selected details. In view of the growing predominance of private laboratories in the genetic/ genomic testing sector, the significance for

future surveys of decisions to withhold details deemed to be “commercial-in-confidence” requires careful deliberation.

6.2.2 Limited Insights into Offshore Testing

One of the survey objectives was to define the volume and nature of genetic/ genomic test requests being sent offshore. Various insights offered by clinical and laboratory colleagues about patient samples known to have been sent overseas – either directly by referring clinicians, pathology laboratories not offering genetic/ genomic testing, or Australian-based collection arms of overseas-based laboratories – revealed that the data on outbound tests were incomplete.

6.3 Comparison with Previous Surveys

This is the third survey of genetic/ genomic testing in Australia. The precedent-setting survey, which was conducted a decade ago, focussed on “molecular” genetic testing.

The second survey, conducted 5 ½ years prior to the 2016/17 survey, was extended to include cytogenetic and biochemical genetic tests but did not include HLA-typing, maternal serum or newborn bloodspot screening. It also sought details about scopes of testing and their associated methodologies, as well as of funding sources.

The 2016/17 survey had much in common with the earlier surveys, although some new items were added. Many of the alterations and additions reflect the changing landscape of genetic/ genomic testing, particularly the expanding range of clinical indications for testing and also of available test methods.

The key differences in the data sought on this occasion were new questions about:

- State-/ Territory-of-origin of test requests. Prompted by the growing phenomenon of interstate and international transfer of samples, this was included with the objective of gaining insights into regional equity of access to genetic/ genomic testing services. As already indicated, this endeavour was thwarted by the concerns of some laboratories about the commercial value of details about referral sources.
- clinical referral sources, as well as a wider range of clinical referral categories. These additions were prompted by the widening spectrum of medical indications for testing.
- types of genetic/ genomic tests offered by laboratories. Additional information was sought so that a more detailed perspective could be offered into the layers of complexity associated with genetic/ genomic testing, including test targeting; genomic resolution; test method selection; interpretive complexity, and the potential clinical relevance of test findings.
- infrastructure for managing the processes of registering test requests and samples; tracking of workflows and samples, and storage of issued reports.
- genomic data storage, in particular details about the infrastructure used for data storage, as well as practices regarding the local storage and retrieval of details about locally identified and curated variants.
- practices regarding the submission of details about locally curated variants to relevant international databases.

6.4 Trends Observed

6.4.1 Changing Patterns of Testing

Major shifts in the relative proportions of completed tests have occurred within several testing categories over the past 5 ½ years – in particular the rates of genetic/ genomic testing categorised previously as “molecular” and “cytogenetic”. The volume of genetic/ genomic testing expanded

during this period by at least 22%,[2] however this rise was limited to the molecular sector, which rose by 73%, while cytogenetic test volumes fell by 40% during the same period.
This represented an ongoing rise in the predominance of molecular testing for both constitutional- and cancer-related testing, although the relative proportions of growth differ within the two sectors. For constitutional- and cancer-related testing, the expansion in molecular testing was 71% and 90%, respectively.

By contrast, the rate of cytogenetic testing (chromosomal karyotyping and fluorescent in-situ hybridisation or FISH) for constitutional disorders fell by 50%, compared with a 13% decline in the cancer-related sector. It should be noted that the documented steep decline in cytogenetic testing for constitutional disorders is coincident with the advent of microarray and massively parallel sequencing. A similar dynamic will be occurring in cancer-related testing; however, the observed lower rate of decline for cancer cytogenetics is due to the ongoing clinical utility and efficiency of chromosomal karyotyping for leukaemia diagnosis, therapy selection and prognosis, as well as the relative cost-effectiveness of FISH-based assessment for predefined oncogenic rearrangements.

6.4.2 Pregnancy-related Screening Tests – Shifting Usage Patterns

Obstetricians, fetal medicine specialists and directors of chemical pathology, cytogenetic and constitutional genetic/ genomic laboratories are well aware of major shifts over recent years in the patterns of clinical requesting for pregnancy-related screening tests. In particular, this includes a rapidly growing rate of non-invasive prenatal screening, an associated major decline in the rate of invasive prenatal tests, a gradual falloff in first trimester (9-13+ weeks) screening and an earlier substantial reduction in the rate of second trimester (14-18 weeks) screening.

The survey findings for pregnancy-related screening tests are in keeping with these observations. It is of interest to note that first trimester biochemical screening or non-invasive prenatal screening was arranged for approximately two thirds of pregnancies in Australia during the survey period.

6.4.3 Expanding Range and Scope of Genetic/ Genomic Tests

The range and scope of genetic/ genomic testing methods continues to expand. The scope of testing now includes targeted assessment for predefined genetic and epigenetic variation, screening for undefined variants in a single gene, screening for undefined variants in a limited number of specified genes, screening for undefined variants in a large number of specified genes, and gene expression profiling.

A wide choice of methods is now available for targeted testing. They include many “molecular” methods, which are dependent on nucleic acid amplification (NAA) by the polymerase chain reaction (PCR). The microscopy-based technique, FISH, is also widely used to assess for targeted genomic/ chromosomal deletions, duplications, structural rearrangements and gene amplifications. As mentioned in section 6.4.1 above, FISH is widely used to assess for predefined oncogenic rearrangements in cancer samples.

Testing can also extend to untargeted screening of all chromosomes (microscopy-based karyotyping), higher-resolution screening of all chromosomes (chromosomal microarray), and massively parallel sequencing, including gene panels, whole exome sequencing and whole genome sequencing. The survey identified the emergence of exome and genome analysis within the constitutional-testing sector, and also the beginnings of cancer-related gene expression analysis.

Specialised genetic, genomic, epigenetic and gene expression tests are now also employed or being introduced. They include targeted testing for microsatellite instability, circulating fetal and

2. *It is expected that this figure substantially underestimates the growth of genetic/ genomic testing due to reasons discussed in Section 5.3.9, particularly differences in the definition of a ‘single test’ across surveys.*

tumour DNA analysis, minimum residual disease and tumour burden analysis, methylation anomalies, uniparental disomy, chimerism, and gene expression profiling.

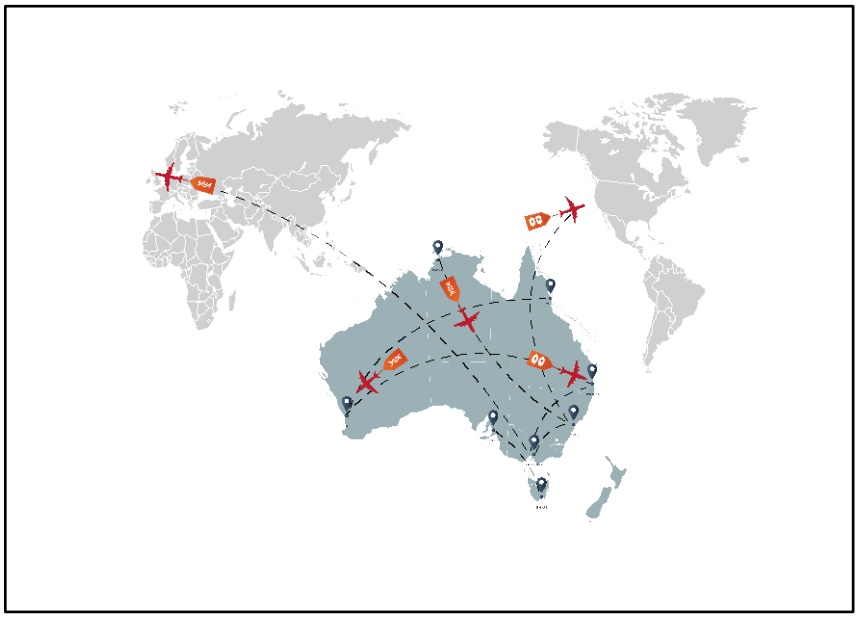
6.4.4 Growing Rate of Interstate Sample Transfers

As previously discussed, analysis of the rates of interstate sample transfers was limited to some extent by gaps in the details provided by laboratories. It was interesting to observe among the data provided that the volume of samples transferred interstate has more than doubled over the past 5 ½ years to an amount likely to be higher than 20%. As expected, the rates of interstate transfer differed among the major test categories, and also for specific tests.

The transfer rate was highest for constitutional genetic/ genomic tests (at least 23% of these patient samples were transferred interstate). Biochemical genetic diagnostic tests were transferred the least. As the highest rates of interstate sample transfer are for genetic/ genomic tests performed by private laboratories, it seems likely that the growing rate of sample transfers is reflecting, to some extent, ongoing consolidation within the private sector.

6.4.5 Growing Rate of International Sample Transfers

The reported number of samples transferred to international laboratories grew by 31% since the last survey, although the total number (3,625) represents less than 1% of all tests. For the reasons summarised in section 6.2.2 above, it is clear that this figure substantially under-represents the total number of overseas referrals.



A useful insight from the limited details gathered about the types of tests referred to overseas laboratories (Table 6), is that a substantial proportion of these tests were present among the numerous tests completed by Australian laboratories during the same time interval (Tables 41 & 42, appendix). The relative prominence of non-invasive prenatal screening tests among the tests sent overseas in 2016/17, which is now offered by several Australian laboratories, serves usefully to illustrate the rapid pace of change associated with offshore test requests.

For incoming test requests, the nature of tests being sought by international requesters appears to reflect a limited number of specific translational-research profiles among several local research and service laboratories.

6.4.6 Genetic/ Genomic Analysis Methods

To accommodate the challenge of detecting genetic/ genomic lesions that may vary by up to 8 orders of magnitude in size, multiple testing methods are utilised by laboratories.

For the task of assaying for predefined genomic variation, a wide variety of nucleic acid amplification techniques (NAAT), both end-point and quantitative, were being used during the survey period. Other methods included FISH, Sanger sequencing, multiplex ligation primer amplification (MLPA), massively parallel sequencing, single nucleotide primer extension, microarray, MALDI-TOF mass spectrometry, Sanger sequencing & MLPA combined, Southern blot analysis, and NAAT & Southern blot combined.

For the task of screening for undefined variants across 1 or 2 genes, the methods being used included Sanger sequencing & MLPA, combined, Sanger sequencing alone, MPS & MLPA combined, and MPS alone. Approximately one third of all laboratories that were accredited to screen multiple genes for undefined variants were using MPS, sometimes with MLPA analysis included.

Nineteen Australian laboratories were continuing to use chromosomal karyotyping, while higher-resolution screening of all chromosomes by microarray was also being offered by a similar number (20) of laboratories. Four laboratories offered whole exome analysis during the survey period, while a single laboratory provided whole genome analysis.

6.4.7 Workforce

The total number of FTEs identified by this survey was 27% higher than the number recorded in 2011. The total is a summation of details provided by all participating laboratories, including Genetic Pathology, Haematology, Anatomical Pathology, Chemical Pathology and Immunopathology laboratories. Inspection of the returns by individual laboratories revealed occasional ambiguities about the proportions of staff time devoted to genetic/ genomic tests within laboratories offering these tests alongside other services pertaining to their major discipline (e.g. Chemical Pathology, Anatomical Pathology, Haematology). These uncertainties will need to be resolved before any firm conclusions can be drawn about total workforce numbers within the sector. It should also be noted that the inclusion of non-accredited laboratories in this survey will have contributed partially to the increased number of FTEs compared to the 2011 survey.

6.4.8 Growing Interpretive Complexity

Genetic/ genomic testing aims to identify variants relevant to a specific phenotype. However, a growing number of tests can now also simultaneously detect additional, or secondary, disease-causing variants that are not directly relevant to the clinical indication for the specified test. Instead, these secondary findings may indicate a heightened risk of either having, or developing in the future, another unrelated condition.[3]

The likelihood of encountering additional disease-associated genomic variants is greatest with whole genome or exome analysis. The risk declines as testing becomes more targeted; however, the genetic phenomenon of pleiotropy[4] leaves open the possibility of identifying genomic changes predisposing to unrelated clinical phenotypes, sometimes even when testing is limited to analysis of a single gene.

3. Further background information about secondary findings is provided in Supplementary Information to the National Health Genomics Policy Framework 2018 – 2021; p14.
4. Refer to Definitions and terminology; Section 2.

Additionally, testing that involves screening specified genomic sequences for undefined variants – as a minimal example, a single tumour suppressor gene – will inevitably identify variants that are of uncertain clinical significance.

With these points in mind, tests were grouped into complexity-associated categories. The largest category was genetic testing targeted to determine whether specified genomic variants were present or absent. Among all constitutional- and cancer-related tests, the overall proportions within this group were 78% and 71%, respectively. Although the defining feature of this category is a mostly binary analytical output (variant present or absent), the grouping fails to take account of the range of post-analytical considerations that may be associated with the subsequent step of interpretive assessment of variants. For example, the clinical interpretations of *HFE* genotypes identified in patients being investigated either because of major iron overload or among healthy first-degree relatives of a newly diagnosed patient can vary substantially. A further example of the challenges associated with binary test outputs is the current emerging trend towards interpretive merging of results from multiple variants, which involves post-analytical summation of the genomic status at each associated risk locus, weighted by the strength of evidence for the specified clinical associations. These types of analyses require numeric validation competencies that are currently not embedded within the curricula for most pathology disciplines.

6.4.9 Genome Informatics

Survey returns revealed that laboratories had widely divergent approaches to the growing challenge of storing patient genomic data. Sixty percent of laboratories indicated that their legacy genomic data were stored on either hospital- or laboratory-based servers. Four laboratories (6%) were uploading patient genomic data into “cloud” storage. Other approaches included use of local and international external data warehouses; clinic servers; research institute and university servers/ tape records; local computer-embedded hard drives; local portable hard drives; digital optical disks (DVDs), and paper records.

Twenty laboratories, or approximately one third of the responding group, indicated dissatisfaction with their arrangements for storing patient genomic data. Points of concern included insufficient storage infrastructure to meet current storage requirements, and insufficient capacity for projected future storage requirements, particularly the minimum duration of retention of bioinformatic genomic data, as stipulated in section 6.7 of the recently revised NPAAC requirements for the retention of laboratory records and patient samples.[5] Other expressed concerns included working with multiple cumbersome arrangements, as well as data insecurity associated with portable hard drive storage.

Open-ended questions about potential solutions and their associated enabling requirements prompted a range of responses (Table 30). Off-site or “cloud” storage was a commonly offered solution. Other suggestions included enabling storage within laboratory information management systems and gaining access to GovNext, a state government storage warehouse.

Commentary

These insights offered by laboratories reveal a considerable range of limitations associated with storage and future accessibility of patient genomic data. Collectively, they are supportive of the summary point below of Australian information systems for genomics, which is included in the Supplementary Information to the National Health Genomics Policy Framework:

> *Communication technologies and improved analytics are rapidly driving Australia’s health system to the cusp of an information-age health system, where genomic data may be better integrated into health care. Internationally, work is being undertaken to develop viable electronic medical record systems capable of handling family history and genomic data required to fully utilise*

5. National Pathology Accreditation Advisory Council Requirements for the Retention of Laboratory Records and Diagnostic Material (Seventh Edition 2018)

> *genomic information for patient care. This recognises that existing clinical informatics architectures are largely incapable of storing genome sequence data in a way that allows the information to be searched, annotated and shared across health care systems over an individual's lifespan.*[6]

6.4.10 International Genomic Database Submissions

Another major genome informatics-related issue was identified among survey responses. Despite the dependence of Australian genomics laboratories on international variant databases for the task of assessing variants of uncertain clinical significance, only one laboratory reported having contributed details of all assessed variants to relevant databases during the survey interval. Overall, approximately three-quarters of genomics laboratories were not contributing details of locally identified genomic variants to international variant databases.

Commentary

As outlined in the National Health Genomics Policy Framework 2018 – 2021,[7] accurate determinations of the clinical significance of genomic variants now requires online access to a comprehensive high-quality knowledge base of all human genomic variants. The reality associated with the current world-wide collection of shared genotypic and phenotypic data is that the data are still far removed from the ideals of being comprehensive and high quality. The survey observation of relatively minimal contributions to international variant databases from Australian genomics laboratories is a source of some discomfort.

6.4.11 Laboratory Supervision

There is a general expectation that laboratories offering a wide range of genetic/ genomic tests, particularly those with the potential to yield complex or challenging results, will be scientifically- and medically-supervised by staff credentialed to deliver effectively the full range of genetic/ genomic tests being delivered. This is addressed in the revised NPAAC Requirements for Supervision in the Clinical Governance of Medical Pathology Laboratories, due to take effect on 1 August 2019, which states that testing must be supervised by a medical practitioner with a relevant Scope of Practice.[8]

Sixty-one of the 81 laboratories offering genetic/ genomic testing indicated availability of either pathologists or scientists with locally-recognised professional qualifications indicating scopes of practice in genetics/ genomics (FRCPA Genetics, FFSc Genetics, FHGSA, recognised overseas qualifications or a combination). Thirty-three laboratories (41%) had access to a genetic pathologist.

At the less supervised end of the spectrum, 21% of laboratories did not have access to any supervising pathologists (FRCPA, any discipline) and 11% did not have either a pathologist (FRCPA, any discipline) or a scientist with a locally-recognised professional qualification indicating proficiency in genetic/ genomic laboratory practice.

Supervision and genetic/ genomic test complexity

With so much variation in the range and number of genetic/ genomic tests performed across laboratories, an assessment was made of the relationship between test volumes within each complexity-associated test category and the professional qualifications of supervising medical and scientific staff.

The observation that a majority of tests in most categories were performed in laboratories with pathologists or scientists with qualifications indicating proficiency in genetic/ genomic testing is

6. Supplementary Information to the National Health Genomics Policy Framework 2018 – 2021; p24.
7. Supplementary Information to the National Health Genomics Policy Framework 2018 – 2021; p25.
8. National Pathology Accreditation Advisory Council Requirements for Supervision in the Clinical Governance of Medical Pathology Laboratories (Fourth Edition 2018)

encouraging. In particular, it suggests that larger laboratories are more likely to have appropriate supervisory arrangements for their genetic/ genomic testing services.

There was, however, one unanticipated exception to this general observation, which involved the category group of targeted screening for undefined variants in smaller gene panels (2-49 genes). For this category, the proportion of all tests completed in the absence of supervisory input from either a pathologist or scientist with genetic/ genomic credentialing was 37% for constitutional tests and 56% for cancer-related investigations. The underlying reasons for this exception were not apparent from the survey returns. It is suggested that the issue of supervision arrangements for more complex genetic/ genomic tests is added to the list of priority areas within the National Health Genomics Policy Framework.

Supervision and genetic/ genomic test methods

Review of the data demonstrating the professional qualifications of supervisory pathologists and scientists against the range of methods within each test scope category offered several additional insights. It is of interest to note that most methods used to assess for the presence or absence of pre-defined variants were supervised by scientists with genetic/ genomic credentialing and pathologists credentialed in other disciplines.

The situation was somewhat different for the methodologies applied to screen for undefined loss-of-function variants in 1 or 2 genes. Although the number of laboratories offering tests within this category was substantially smaller than those involved with targeted testing, it was interesting to observe a generally more comprehensive approach to screening these genes for inactivating variants among the laboratories supervised by pathologists credentialed in genetics/ genomics. In particular, more of these laboratories were offering both sequencing and allele copy number analysis of genes, rather than sequencing alone. From a clinical perspective, the more comprehensive approach delivers a higher yield of disease-associated variants (test sensitivity), with an accompanying gain in the post-test negative predictive value of these tests.

As expected, among the relatively small number of laboratories offering tests that involve screening for undefined variants in large panels (more than 50 specified genes) or exomes, there was a prominence of either pathologists or scientists with genetic/ genomic credentialing. There were, however, several laboratories offering large panel tests or exome screening without support from a genetic pathologist or a genetically credentialed scientist.

6.4.12 Reporting (Turnaround) Times

Building on the 2011 survey precedent of including an assessment of reporting times, the topic was evaluated in greater detail in this survey.

Turnaround times were available for 74% of all test group summaries provided by laboratories. This is considerably lower than the 94% level achieved in the 2011 survey. Feedback from several laboratories unable to provide reporting times indicated that the decline is likely reflecting a co-occurrence of several factors – the limited capabilities of many extant information management systems, as discussed in section 6.2.1 above, increasing staff workloads arising from increasing clinical demand for genetic/ genomic testing, as well as growing analytical and interpretive complexity associated with the range of tests now being requested.

Median, 90th centiles and ranges of all available reporting times were summarised for each major test category. Comparison with the equivalent median values presented in the 2011 survey offers some useful insights. The median reporting times for targeted molecular assays has improved substantially over the past 5 ½ years. This improvement is encouraging and seems likely to be reflecting an ongoing streamlining of molecular testing processes within laboratories. It should be

noted, however, that the range of reporting times around these median values was broad. Many laboratories delivered a substantial proportion of their results later than the reporting times recommended by the UK's Association for Clinical Genetic Science.[9]

The same is true for microarray analysis for which median reporting times have also improved substantially between surveys. The range of reporting times for microarray, however, is wide with a substantial proportion exceeding substantially the UK's recommended reporting time targets.

It should be noted that as a result of an oversight involving the questions about fetal tissue analysis, it was not possible to distinguish fetal samples obtained from invasive antenatal procedures and fetal post mortems. As a result, it was not possible to provide summaries of reporting times for the different categories of tests involving fetal samples. The median reporting times for cytogenetic analysis of samples, both for constitutional- and cancer-related purposes, remains essentially unchanged from the times reported in the 2011 survey. It was apparent, however, that the 90th centile reporting times for constitutional- and cancer-related cytogenetic testing were 22 and 21 days, respectively, both of which exceed the current recommended standard for Australian laboratories.[10]

The median reporting times for molecular constitutional- and cancer-related tests involving screening genes for unknown disease-causing mutations have deteriorated. It seems likely that a range of reasons underlie this observed deterioration, including growing clinical demand for tests in this category, and increasing analytical and interpretative complexity, particularly for larger gene panels.

6.4.13 Funding Arrangements

The 2016/17 survey data revealed significant shifts over the past 5 ½ years in the funding arrangements for genetic/ genomic tests. For within-state tests, federal funding (Medicare) covered almost half (49%) of tests in 2016/17, compared with approximately 35% in 2011. There have been corresponding falls in the proportion of within-states tests funded by the state (31% of all tests in 2016/17) and by patients (16%).

Survey data revealed several notable differences in funding arrangements for samples that had been transferred across state borders for testing compared with tests performed locally. Federal funding covered a higher proportion (approximately two thirds) of interstate tests, with most of these being performed by private laboratories. Additionally, while the percentage of within-state tests funded directly by patients has fallen since 2011, the proportion of interstate tests paid for by patients has doubled to approximately a quarter of these tests. This is largely reflective of the growing uptake of non-invasive prenatal screening for chromosomal aneuploidies which, during the 2016/17 financial year, was offered by only a few Australian laboratories.

The listing of new test items on the Medicare Benefits Schedule (MBS) is subject to the assessment and approval processes of the Medical Services Advisory Committee (MSAC). The MBS currently includes approximately 50 items applicable to constitutional or cancer (somatic) genetic/ genomic testing;[11] however, approximately ten items have been added since the 2016/17 survey window. Although the number of tests funded by Medicare is relatively small, most high volume tests identified by the survey were associated with a Medicare rebate (Tables 13 and 14), and a further high volume test, cystic fibrosis, has recently been added to the MBS in the form of six new items covering a range of clinical referral scenarios. The overall proportions of constitutional and cancer

9. General Genetic Laboratory Reporting Recommendations, Association for Clinical Genetic Science, February 2015.
10. National Pathology Accreditation Advisory Council. Requirements for Cytogenetic Testing (Third Edition 2013).
11. MBS Online (1 November 2018). Available at: http://www.mbsonline.gov.au

tests covered by federal funding in 2016/17 were broadly similar; however, biochemical genetic testing continues to be predominantly state-funded (Figures 11-13).

6.4.14 Survey data retention

The 2016/17 survey was commissioned to provide a baseline for future ongoing monitoring and reporting of progress against the priorities of the National Health Genomics Policy Framework, particularly to identify gaps and immediate priorities for implementation. The survey on this occasion used secure storage provided by the RCPA, within which the raw data submissions will continue to be retained on an ongoing basis, unless agreed by Health, for any additional analyses; validation; assistance required for planning of future surveys, and also to form the basis for a longitudinal data set.

Appendix A

Methods

As a range of different cyto-molecular testing methods can be used for most of the test scope categories, table 40 lists the methods that were being used by Australian laboratories during the 2016/17 financial year, as well as the numbers of laboratories using each of test methods listed. The table offers insights into the numbers of laboratories using each of the methods listed, as well as the number of Australian laboratories offering tests within each of the scope categories.

Table 40: Methods applied within test scope categories offered by laboratories

Test scope category	Laboratory category				Laboratories using test method within each test scope category
	Constitutional		Cancer		
Test method	Service	Research	Service	Research	
Targeted testing for presence/ absence of predefined genomic variation					**Totals**
NAAT (end-point)	28	1	20	1	**50**
NAAT (quantitative, excl. ddPCR)	12	-	20	1	**33**
FISH	12	-	18	-	**30**
Sanger sequencing	11	4	6	1	**22**
MLPA	16	-	4	1	**21**
Massively parallel sequencing	10	-	7	-	**17**
Single nucleotide primer extension	2	-	6	-	**8**
Microarray	8	-	-	-	**8**
ddPCR	-	-	5	1	**6**
MALDI-TOF	3	-	2	-	**5**
Sanger sequencing & MLPA	5	-	-	-	**5**
Southern blot	3	-	-	-	**3**
NAAT (end-point) & Southern blot	2	-	-	-	**2**
Targeted screening for undefined variants in 1 or 2 genes					
Sanger sequencing	15	4	-	-	**19**
Sanger sequencing & MLPA	9	1	2	-	**12**
Massively parallel sequencing	8	1	-	-	**9**
MPS & MLPA	6	-	-	-	**6**
Targeted screening for undefined variants in 3 – 50 genes					
Sanger sequencing	5	-	-	-	**5**
Sanger sequencing & MLPA	3	-	-	-	**3**
Massively parallel sequencing	12	2	6	1	**21**
MPS & MLPA	9	-	-	-	**9**
Targeted screening for undefined variants in more than 50 specified genes					
Massively parallel sequencing	8	2	2	1	**13**
Untargeted screening of all chromosomes (karyotyping)					
Microscopy	15	-	11	-	**26**
Untargeted higher-resolution screening of all chromosomes					
Microarray	18	-	6	-	**24**
Untargeted screening of whole exome					
Massively parallel sequencing	4	1	-	-	**5**

There are now several thousand different genetic/ genomic tests available that have clinical utility. The tests performed during the 2016/17 financial year are listed below in two tables. Tables 41 and 42 list the total number of constitutional- and cancer-related tests, respectively, completed in the 12-month period.

Note, there are several tests assaying for different classes of mutation within a single gene.

Table 41: Constitutional cyto-molecular tests (all states and territories)

Test groups Test name	No. of tests
"Genome scale" testing	
Chromosomal karyotyping	55613
Chromosomal microarray analysis	42175
Whole Exome Sequencing	775
Whole Genome Sequencing	346
Targeted genomic loci or chromosomal regions	
Aneuploidy Screening (maternal blood – fetal DNA)	55789
Aneuploidy Screening (pre-implantation aneuploidy screening)	11981
Aneuploidy Screening (targeted family follow-up)	5920
Aneuploidy Screening (rapid prenatal – fetal tissues)	4789
Aneuploidy Screening (genetic screening – population risk)	239
Constitutional deletions/ duplications/ rearrangements identifiable using molecular technologies	2108
Linkage/ Phasing Studies (family linkage, segregation, "trio", etc.)	1692
Maternal Cell Contamination *(analysists noted under-reporting of MCC)*	805
Identity testing (medical reasons)	673
Chimerism analysis	400
Uniparental disomy (UPD)	157
Molar pregnancy (genotyping)	54
X-Inactivation Studies	28
Zygosity Studies	23
Targeted family-specific gene variant	
Family predictive/ cascade testing	2392
Targeted Multi-Gene Panels (gene-focussed tests involving 3 or more genes)	
CARDIOVASCULAR	
Panel – Arrhythmia (11-50 genes)	96
Panel – Arrhythmia (51+ genes)	10
Panel – Aortopathy	159
Panel – Cardiac (11-50 genes)	403
Panel – Cardiac (51+ genes)	461
Panel – Cardiomyopathy (11-50 genes)	86

Test groups Test name	No. of tests
Panel – Cardiomyopathy (51+ genes)	159
Panel – Familial hypercholesterolemia, LDLR, APOB & PCSK9	306
Panel – Marfan syndrome	12
HEREDITARY CANCER	
Panel – Breast and Ovarian (3-50 genes)	2401
Panel – Breast and Ovarian (51+ genes)	776
Panel – Cancer, indeterminate (11-50 genes)	78
Panel – Cancer, comprehensive/ indeterminate (51+ genes)	40
Panel – Colorectal/ endometrial/ ovarian (3-10 genes)	416
Panel – Colorectal/ endometrial/ ovarian (11+ genes)	297
Panel – Multiple endocrine neoplasia	14
Panel – Phaeochromocytoma/ Paraganglioma	64
Panel – Polyps	38
NEUROMUSCULAR DISEASES	
Panel - Ataxia	8
Panel – CADASIL	2
Panel – Epilepsy	119
Panel – Hereditary spastic paraplegia	35
Panel – Neuromuscular	406
Panel – Parkinsonism	3
Panel – Peripheral Neuropathy	3
OTHER	
Panel – Ashkenazi Jewish Disease Genes	626
Panel – aHUS	10
Panel – Angelman/ Absent speech	41
Panel – Autoimmune disease	6
Panel – Bleeding disorders	6
Panel – Blood group typing	78
Panel – Brittle bone disorders	106
Panel – Ciliopathy	32
Panel – Cohesinopathies	23
Panel – Craniosynostosis/ Skeletal dysplasia	63
Panel – Deafness/ Hereditary Hearing Loss	8
Panel – Disorders of Sexual Development	38
Panel – Epidermolysis bullosa	16
Panel – Endocrine	28
Panel – Eye diseases	145
Panel – Familial hypercholesterolemia	3
Panel – Familial Hyperinsulinism	13
Panel – Fanconi anaemia	2
Panel – Haematological disorders	17
Panel – Hereditary haemorrhagic telangiectasia	3
Panel – HLA (comprehensive sequencing)	11470
Panel – Hydrops fetalis	14
Panel – Hyperparathyroidism	2

Test groups Test name	No. of tests
Panel – Immunological diseases	55
Panel – Inborn errors of metabolism (targeted variants across several genes)	210
Panel – Inborn errors of metabolism (gene panel sequencing)	36
Panel – Infertility	268
Panel – Maturity-onset diabetes of the young (MODY)	167
Panel – Migraine	45
Panel – Mitochondrial, MERRF/MELAS/NARP	1134
Panel – Mucopolysaccharidoses (targeted variants across multiple genes)	41
Panel – Neutropenia	3
Panel – Noonan and RASopathy Panel	160
Panel – Overgrowth	33
Panel – Periodic fever syndromes	57
Panel – Pharmacogenomics (targeted variants across multiple genes)	4007
Panel – Porphyria (FECH, HMBS, UROD, CPOX, UROS & PPOX)	19
Panel – Pre-pregnancy carrier screening	280
Panel – Renal diseases	222
Panel – Retinal dystrophies	41
Panel – Sarcoma	5
Panel – Skin	30
Panel – Spinocerebellar ataxia (all types)	481
Panel – Surfactant protein deficiency (ABCA3, SFTPB, SFTPC, NKX2-1)	76
Panel – Usher syndrome	2
Panel – Xeroderma pigmentosum	2
Panel – "Untargeted" disease gene panel (e.g. TruSight One)	171
Panel – Miscellaneous	357

Tests for conditions usually involving 1 or 2 genes (Listed alphabetically – see below for test frequency listing)	
5α-reductase, SRD5A2	3
α1-antitrypsin	4385
ACAM/MCAD	21
Achondroplasia, FGFR3	34
ACTA2 gene	1
Acyl co-enzyme A dehydrogenase, ACADM	4
Agammaglobulinaemia, X-linked	8
aHUS, DGKE	3
AIRE (gene common variants)	5
Angelman syndrome	170
Anosmia, familial	1
APC Promoter (GAPPS)	50
APOE gene	693
ARX gene	26
Barth syndrome, TAZ	4
Basal cell nevus syndrome	1
Batten disease	44
Beckwith syndrome	149
Birt Hogg Dube syndrome	49
Bleeding disorders	29
Blood group typing	1179
BMPR1A / SMAD4	34
BRCA1 & BRCA2 (MBS item)	2939
Breast Cancer (Jewish)	16
Breast/ ovarian cancer	10
BTK gene	3
C4, copy number	32
CADASIL (single genes/ targeted variants)	207
Cancer, indeterminate (single genes/ targeted variants)	85
Cardiac, indeterminate (single genes/ targeted variants)	45
Cardiomyopathy, dilated, RBM20	6
Cardiomyopathy, dilated, TTN	5
CASR gene	84
CDC73/HRPT2	3
CDH1 gene	5
CDKN1B beta/MEN4	2
Charcot Marie Tooth, type 1B/MPZ	10
Charcot-Marie-Tooth Type 2/MFN3	14
Charcot-Marie-Tooth type Type X1/GJB1	23
CHARGE syndrome, CDH7	16
Chemokine receptor type 5, CCR5-delta 32	88
Chronic granulomatous disease	8
Chronic mucocutaneous candidias	3
Coeliac	7482
Collagenopathies, type 2	4
Colorectal/ endometrial/ ovarian	520
Colorectal cancer, MUTYR	183
Congenital Adrenal Hyperplasia, CYP21A2	132
CYP11B1 and CYP11B2 hybrid	97
CYP24A1	5
CYP2C19 gene	130

Tests for conditions usually involving 1 or 2 genes (Listed alphabetically – see below for test frequency listing)	
CYP2C9 gene	90
CYP2D6 gene	218
CYP3A5/CYP3A4 genes	38
Cryopyrin-Associated Periodic Syndrome, NLRP3	25
Cystic fibrosis, CFTR	17126
Cytochrome P450	1046
DAZ gene	300
DDX41 gene	11
Deafness	638
DFBN1 gene	89
DPYD gene	8
Drash syndrome	4
Dravet syndrome	42
DRPLA	55
Duchenne/Becker Muscular Dystrophy, DMD	346
Ehlers Danlos syndrome, COL3A1	16
Epileptic encephalopathy, early infantile, CDKL5	2
Fabry disease	30
Facioscapulohumeral Muscular Dystrophy	95
Factor V Leiden, or other variants relevant to DVT/PE (MBS item)	41815
Factor XII gene	46
Familial cold autoinflammatory syndrome	4
Familial hypocalciuric hypercalcaemia 3 (FHH3)	4
Familial Mediterranean fever, MEFV	383
Familial motor neurone disease, C9orf72	152
Familial motor neurone disease, SOD1	16
Familial motor neurone disease, TARDBP	4
Familial polyposis coli (APC)	255
FGFR2 gene	2
FOXL2 gene	1
FOXP3 gene	1
Fragile X Syndrome, FMR1 triplet repeat (MBS item)	17832
Friedreich ataxia, FXN	237
Fumarate Hydratase deficiency, FH	3
Galactosemia, GALT	4
Gastric	20
GATA2 gene	1
Gilbert syndrome, UGT1A	318
GNAS-associated imprinting disorders	3
Haemophagocytic lymphohistiocytosis	5
Haemophilia A, F8	270
Haemophilia A, F9	21
Herditary fructose intolerance	2
Hereditary angioedema, SERPING1	15
Hereditary Pancreatitis, PRSS1	18
Hereditary Pancreatitis, SPINK1	9
Hereditary sensory neuropathy type IA/SPTLC1	8
Hereditary spastic paraplegia	35
HFE gene (MBS item)	75170

Tests for conditions usually involving 1 or 2 genes (Listed alphabetically – see below for test frequency listing)	
HLA B27 (MBS item)	36615
HLA B5 or B51	84
HLA B5701 (Abacavir therapy) (MBS item)	1444
HLA B5801	40
HLA DR/DQ	20403
HLA typing (carbamazepine hypersensitivity)	22
HNF1B gene	6
Huntington disease, HD	839
Hyper IgE Syndrome	15
Hyperparathyroidism	3
Hypophosphatasia, ALPL	13
IKBKG gene	21
Inborn errors of metabolism (miscellaneous single genes)	451
JAG1 gene	24
Juvenile polyposis	2
Kennedy disease, AR	55
Laminopathies	5
LCHAD deficiency, HADHA	5
Legius Syndrome, SPRED1	3
Li Fraumeni syndrome	67
LTBP2 gene	1
Lymphedema distichiasis syndrome, FOXC2	1
Lymphoproliferative, autoimmune	5
Malignant hyperthermia, RYR1	1
Marfan syndrome, FBN1	89
MAX gene	2
Melanoma	26
MELAS (mtDNA)	16
MEN1 gene	97
MEN2 (RET germline mutations) (MBS item)	35
MERRF (mtDNA)	3
Migraine	5
MLH1 gene	142
MSH2 gene	141
MSH6 gene	73
MTHFR gene	16803
Myotonic dystrophy, DM1	630
Myotonic dystrophy, DM2	43
Nephrotic syndrome, NPH+C598S1/ NPH	3
Neurofibromatosis type 1, NF1	17
Neurofibromatosis type 2, NF2	95
Neuropathy, peripheral, PMP22 (MBS item)	345
Oculopharyngeal muscular dystrophy, PABPN1	20
Osteogenesis imperfecta, COL1A1 & COL1A2	57
OTC gene	14
Palmoplantar keratoderma	2
Parkinson disease, LRRK2	8
PAX6 gene	5
Periodic fever syndromes	6
Phenylketonuria, PAH	9
PHOX2B gene	13

Tests for conditions usually involving 1 or 2 genes (Listed alphabetically – see below for test frequency listing)	
PMS2 gene	1
POLG gene	16
Prader Willi Syndrome	302
Prothrombin, F2	40815
Pompe disease	11
PTEN gene	53
PTH gene	1
Retinoblastoma	77
Retinal dystrophies (various)	80
RET gene	44
Rett Syndrome, MECP2	69
Rhabdoid tumour syndrome	40
RHCE Genotyping	86
RHD Genotyping	653
Rheumatoid arthritis-associated motif	47
Russell Silver Syndrome	141
Schwannomatosis	10
SDHA gene	5
SDHB gene	20
SDHC gene	8
SDHD gene	17
Severe combined immunodeficiency, X-linked, IL2RG	8
SHOX gene	66
Simpson Golabi Behmel syndrome	1
SLC26A4 gene	1
SMAD3 gene	22
Stickler Syndrome, Spondyloepiphyseal Dysplasia Congenita (COL2A1)	8
Spinal muscular atrophy	5154
STK11 gene	28
SURF1 gene	2
Thalassaemia (alpha)	12092
Thalassaemia (beta)	1449
Thalassaemia (alpha and beta)	238
Thyroid hormone resistence, THRB	6
TMEM127 gene	2
TNFRSF1A-associated periodic syndrome	58
Thiopurine S-methyltransferase (TPMT)	8684
TTR gene	1
VDR gene	1
Venoocclusive disease, VOD, SP110	2
Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency, ACADVL	7
VKORC1 gene	1059
Von Hippel-Lindau syndrome (VHL)	79
Wilms tumour (bilateral)	16
Wilson syndrome	12
Wiskott-Aldrich syndrome	11
Wolfram syndrome	6
Miscellaneous	4902

Tests for conditions usually involving 1 or 2 genes (Listed by descending order of test frequency)	
HFE gene (MBS item)	75170
Factor V Leiden, or other variants relevant to DVT/PE (MBS item)	41815
Prothrombin, F2	40815
HLA B27 (MBS item)	36615
HLA DR/DQ	20403
Fragile X Syndrome, FMR1 triplet repeat (MBS item)	17832
Cystic fibrosis, CFTR	17126
MTHFR gene	16803
Thalassaemia (alpha)	12092
Thiopurine S-methyltransferase (TPMT)	8684
Coeliac	7482
Spinal muscular atrophy	5154
Miscellaneous	4902
α1-antitrypsin	4385
BRCA1 & BRCA2 (MBS item)	2939
Thalassaemia (beta)	1449
HLA B5701 (Abacavir therapy) (MBS item)	1444
Blood group typing	1179
VKORC1 gene	1059
Cytochrome P450	1046
Huntington disease, HD	839
APOE gene	693
RHD Genotyping	653
Deafness	638
Myotonic dystrophy, DM1	630
Colorectal/ endometrial/ ovarian	520
Inborn errors of metabolism (miscellaneous single genes)	451
Familial Mediterranean fever, MEFV	383
Duchenne/Becker Muscular Dystrophy, DMD	346
Neuropathy, peripheral, PMP22 (MBS item)	345
Gilbert syndrome, UGT1A	318
Prader Willi Syndrome	302
DAZ gene	300
Haemophilia A, F8	270
Familial polyposis coli (APC)	255
Thalassaemia (alpha and beta)	238
Friedreich ataxia, FXN	237
CYP2D6 gene	218
CADASIL (single genes/ targeted variants)	207
Colorectal cancer, MUTYR	183
Angelman syndrome	170
Familial motor neurone disease, C9orf72	152
Beckwith syndrome	149
MLH1 gene	142
MSH2 gene	141
Russell Silver Syndrome	141
Congenital Adrenal Hyperplasia, CYP21A2	132
CYP2C19 gene	130
CYP11B1 and CYP11B2 hybrid	97
MEN1 gene	97
Facioscapulohumeral Muscular Dystrophy	95
Neurofibromatosis type 2, NF2	95
CYP2C9 gene	90
DFBN1 gene	89
Marfan syndrome, FBN1	89

Tests for conditions usually involving 1 or 2 genes (Listed by descending order of test frequency)	
Chemokine receptor type 5, CCR5-delta 32	88
RHCE Genotyping	86
Cancer, indeterminate (single genes/ targeted variants)	85
CASR gene	84
HLA B5 or B51	84
Retinal dystrophies (various)	80
Von Hippel-Lindau syndrome (VHL)	79
Retinoblastoma	77
MSH6 gene	73
Rett Syndrome, MECP2	69
Li Fraumeni syndrome	67
SHOX gene	66
TNFRSF1A-associated periodic syndrome	58
Osteogenesis imperfecta, COL1A1 & COL1A2	57
DRPLA	55
Kennedy disease, AR	55
PTEN gene	53
APC Promoter (GAPPS)	50
Birt Hogg Dube syndrome	49
Rheumatoid arthritis-associated motif	47
Factor XII gene	46
Cardiac, indeterminate (single genes/ targeted variants)	45
Batten disease	44
RET gene	44
Myotonic dystrophy, DM2	43
Dravet syndrome	42
HLA B5801	40
Rhabdoid tumour syndrome	40
CYP3A5/CYP3A4 genes	38
Hereditary spastic paraplegia	35
MEN2 (RET germline mutations) (MBS item)	35
Achondroplasia, FGFR3	34
BMPR1A / SMAD4	34
C4, copy number	32
Fabry disease	30
Bleeding disorders	29
STK11 gene	28
ARX gene	26
Melanoma	26
Cryopyrin-Associated Periodic Syndrome, NLRP3	25
JAG1 gene	24
Charcot-Marie-Tooth type Type X1/GJB1	23
HLA typing (carbamazepine hypersensitivity)	22
SMAD3 gene	22
ACAM/MCAD	21
Haemophilia A, F9	21
IKBKG gene	21
Gastric	20
Oculopharyngeal muscular dystrophy, PABPN1	20
SDHB gene	20
Hereditary Pancreatitis, PRSS1	18
Neurofibromatosis type 1, NF1	17
SDHD gene	17
Breast Cancer (Jewish)	16
CHARGE syndrome, CDH7	16
Ehlers Danlos syndrome, COL3A1	16

Tests for conditions usually involving 1 or 2 genes (Listed by descending order of test frequency)	
Familial motor neurone disease, SOD1	16
MELAS (mtDNA)	16
POLG gene	16
Wilms tumour (bilateral)	16
Hereditary angioedema, SERPING1	15
Hyper IgE Syndrome	15
Charcot-Marie-Tooth Type 2/MFN3	14
OTC gene	14
Hypophosphatasia, ALPL	13
PHOX2B gene	13
Wilson syndrome	12
DDX41 gene	11
Pompe disease	11
Wiskott-Aldrich syndrome	11
Breast/ ovarian cancer	10
Charcot Marie Tooth, type 1B/MPZ	10
Schwannomatosis	10
Hereditary Pancreatitis, SPINK1	9
Phenylketonuria, PAH	9
Agammaglobulinaemia, X-linked	8
Chronic granulomatous disease	8
DPYD gene	8
Hereditary sensory neuropathy type IA/SPTLC1	8
Parkinson disease, LRRK2	8
SDHC gene	8
Severe combined immunodeficiency, X-linked, IL2RG	8
Stickler Syndrome, Spondyloepiphyseal Dysplasia Congenita (COL2A1)	8
Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency, ACADVL	7
Cardiomyopathy, dilated, RBM20	6
HNF1B gene	6
Periodic fever syndromes	6
Thyroid hormone resistence, THRB	6
Wolfram syndrome	6
AIRE (gene common variants)	5
Cardiomyopathy, dilated, TTN	5
CDH1 gene	5
CYP24A1	5
Haemophagocytic lymphohistiocytosis	5
Laminopathies	5
LCHAD deficiency, HADHA	5
Lymphoproliferative, autoimmune	5
Migraine	5
PAX6 gene	5
SDHA gene	5
Acyl co-enzyme A dehydrogenase, ACADM	4
Barth syndrome, TAZ	4
Collagenopathies, type 2	4
Drash syndrome	4
Familial cold autoinflammatory syndrome	4
Familial hypocalciuric hypercalcaemia 3 (FHH3)	4
Familial motor neurone disease, TARDBP	4
Galactosemia, GALT	4
5α-reductase, SRD5A2	3
aHUS, DGKE	3

Tests for conditions usually involving 1 or 2 genes (Listed by descending order of test frequency)	
BTK gene	3
CDC73/HRPT2	3
Chronic mucocutaneous candidias	3
Fumarate Hydratase deficiency, FH	3
GNAS-associated imprinting disorders	3
Hyperparathyroidism	3
Legius Syndrome, SPRED1	3
MERRF (mtDNA)	3
Nephrotic syndrome, NPH+C598S1/ NPH	3
CDKN1B beta/MEN4	2
Epileptic encephalopathy, early infantile , CDKL5	2
FGFR2 gene	2
Herditary fructose intolerance	2
Juvenile polyposis	2
MAX gene	2
Palmoplantar keratoderma	2
SURF1 gene	2
TMEM127 gene	2
Venoocclusive disease, VOD, SP110	2
ACTA2 gene	1
Anosmia, familial	1
Basal cell nevus syndrome	1
FOXL2 gene	1
FOXP3 gene	1
GATA2 gene	1
LTBP2 gene	1
Lymphedema distichiasis syndrome, FOXC2	1
Malignant hyperthermia, RYR1	1
PMS2 gene	1
PTH gene	1
Simpson Golabi Behmel syndrome	1
SLC26A4 gene	1
TTR gene	1
VDR gene	1

Table 42: Cancer cyto-molecular tests (all states and territories)

Test groups	Tests	No. of tests
"Genome scale" testing		
	Chromosomal karyotyping	20102
	Chromosomal microarray analysis	1436
	Gene expression studies	179
Targeted genomic loci or chromosomal regions		
	Chimerism analysis	4133
	Aneuploidy Screening (tumour tissues/ cells)	1115
	Microsatellite Instability (MSI/ MMR) Studies	556
	Loss of heterozygosity studies (microsatellites)	21
Transplant HLA typing		
	Panel – HLA (comprehensive sequencing)	5000
Targeted Multi-Gene Panels (gene-focussed tests involving 3 or more genes)		
	Panel – Breast/ Ovarian cancer (3-10 genes)	2

Test groups	Tests	No. of tests
	Panel – Breast/ Ovarian cancer (11-50 genes)	78
	Panel – Cancer (11-50 genes)	572
	Panel – Colorectal cancer (3-10 genes)	39
	Panel – Colorectal cancer (11-50 genes)	615
	Panel – Gastric cancer (11-50 genes)	48
	Panel – Lung cancer (11-50 genes)	553
	Panel – Lung/ Melanoma/ Colorectal (3-10 genes)	124
	Panel – Lung/ Melanoma/ Colorectal (11-50 genes)	350
	Panel – Lung/ Thyroid Fusion Profile (3-10 genes)	5
	Panel – Melanoma (3-10 genes)	26
	Panel – Melanoma (11-50 genes)	386
	Panel – Myelodysplastic Syndrome/ Leukaemia (51-100 genes)	697
	Panel – Cancer, comprehensive (51-100 genes)	50
	Panel – Cancer, comprehensive (101-200 genes)	150
	Panel – Cancer, comprehensive (400+ genes)	50
	Panel – Cancer, indeterminate (101-200 genes)	250
	Panel – Lymphoid malignancies (51-100 genes)	466
	Panel – Myeloid malignancies (11-50 genes)	5
	Panel – Myeloid malignancies (51-100 genes)	688
Targeted testing *(loci; specific gene variants or regional chromosomal regions)*		
	(Listed alphabetically – see below for test frequency listing)	
	Aneurysmal Bone Cyst and Nodular Fasciitis, USP6	17
	Brain, 1p/19q co-deletion	166
	Brain, BRAF fusion	31
	Brain, BRAF V600	44
	Brain, EGFR	55
	Brain, IDH1	279
	Brain, IDH2	107
	Brain, MGMT	34
	Brain, MYC	22
	Breast, ERBB2 (HER2)	2333
	Cancer, indeterminate (targeted variants)	201
	Colorectal, BRAF V600	825
	Colorectal, KRAS	125
	Colorectal, NRAS	72
	Colorectal, KRAS & NRAS	1512
	Colorectal, targeted variants (unspecified)	1569
	Colorectal/ Endometrial, MLH1 promoter	515
	Endometrial cancer, BRAF V600	12
	Gastric cancer, ERBB2 (HER2)	114
	Gastrointestinal stromal tumour, KIT	24
	Gastrointestinal stromal tumour, PDGFRA	7
	Gastric cancer, miscellaneous oncogenic mutations	2
	Glioblastoma, MGMT	7
	Haematological disorders, CRLF2, MYC, CCND1, TP53, XY, enumeration probes	90
	IGH hypermutation	12
	Langerhans cell histiocytosis, BRAF V600	3

Test groups	Tests	No. of tests
	Leukaemia, acute lymphoid, minimal residual disease testing	755
	Leukaemia, acute lymphoid, CRLF2; CEP4/10/17; BCR/ABL1; KMT2A; TCF3/PBX1/HLF; ETV6/RUNX1 rearr.	49
	Leukaemia, acute lymphoid, KMT2A (MLL) rearrangement	425
	Leukaemia, acute lymphoid, t(12;21) ETV6-RUNX1	481
	Leukaemia, acute lymphoid, miscellaneous oncogenic mutations	39
	Leukaemia, acute myeloid, CBFB rearrangement	487
	Leukaemia, acute myeloid, CEBPA	169
	Leukaemia, acute myeloid, FLT3	1846
	Leukaemia, acute myeloid, FLT3 & NPM1	194
	Leukaemia, acute myeloid, IDH1/ IDH2	56
	Leukaemia, acute myeloid, KIT	256
	Leukaemia, acute myeloid, NPM1	767
	Leukaemia, acute myeloid, t(15;17) PML-RARA	1414
	Leukaemia, acute myeloid, t(8;21) RUNX1T1-RUNX1	1304
	Leukaemia, CDKN2A/D9Z3	25
	Leukaemia, chronic lymphoid, miscellaneous rearrangements	160
	Leukaemia, chronic myeloid, IGHV somatic hypermutation	73
	Leukaemia, CRLF2 rearr.	17
	Leukaemia, D4Z1/D10Z1/D17Z1	12
	Leukaemia, D6Z1/SEC63/MYB	1
	Leukaemia, epsinophilic, FGFR3, FIP1L1-CHIC2-PDGFRA, PDGFRB rearr.	11
	Leukaemia, ETV6 rearr.	4
	Leukaemia, hairy cell, BRAF	5
	Leukaemia, hairy cell, KIT	6
	Leukaemia, IKZF1	4
	Leukaemia, PBX1/HLF/TCF3	0
	Leukaemia, RARA (5'3')	5
	Leukaemia, t(4;14), KMT2A-AFF1	1
	Leukaemia, t(9;11) KMT2A-MLLT3	2
	Leukaemia, t(9;22) BCR-ABL1	18715
	Leukaemia, TLX3 rearr.	10
	Leukaemia/ MDS MECOM (3'5')	31
	Leukaemia/ MDS, D7Z1/KMT2E/MET	33
	Leukaemia/ Sarcoma FUS rearr.	17
	Leukaemia/ Solid tumour rearrangements (various)	226
	Liposarcoma, 12q15	79
	Liposarcoma, MDM2	110
	Liposarcoma, myxoid,12q13 rearr.	10
	Lung cancer, miscellaneous targeted variants	2620
	Lung, ALK	779
	Lung, EGFR	4203
	Lung, KRAS	218
	Lung, ROS1	264
	Lymphoma, ALK rearrangement	17
	Lymphoma, ATM/TP53	474
	Lymphoma, BCL2 rearrangement	498

Test groups	Tests	No. of tests
	Lymphoma, BCL6 rearrangement	470
	Lymphoma, Burkitt, 8q24/14q32)	19
	Lymphoma, Clonality (IGH/ IGK Gene Rearrangement Analysis)	841
	Lymphoma, Clonality (T-Cell Receptor Gene Rearrangement Analysis)	1653
	Lymphoma, DUSP22 rearr.	2
	Lymphoma, IGK rearr.	2
	Lymphoma, IGL rearr.	1
	Lymphoma, IRF4 rearr.	123
	Lymphoma, MALT1 rearrangement	113
	Lymphoma, MYC rearrangement	716
	Lymphoma, NPM-ALK rearr.	24
	Lymphoma, t(11;14) CCND1-IGH@	414
	Lymphoma, t(14;18) BCL2-IGH@	244
	Lymphoma, t(8;14) IGH-MYC	113
	Lymphoma, TP63 rearr.	1
	Lymphoma/ Leukaemia, TCL1A rearr.	8
	Lymphoma/ MDS/ MPN, RB1/DLEU2/LAMP1	196
	Lymphoma/ Myeloma, CCND1 rearr.	7
	Lymphoma/ Myeloma, IGH rearr.	5
	Lymphoma/ Myeloma, MYC rearr.	96
	Lymphoma/ Myeloma, t(6;14) CCND3-IGH	1
	Lymphoma/ Myeloma, t(8;14) MYC-IGH	43
	Lymphoma/ Sarcoma D12Z3/MDM2	378
	MDS, D5S1518E-D5S1976/EGR1/RPS14	37
	MDS, PTPRT/20qter	10
	MDS, SCFD2/TET2	8
	MDS/ MPN/ Leukaemia, CALR	1569
	MDS/ MPN/ Leukaemia, FGFR1 rearr.	8
	MDS/ MPN/ Leukaemia, JAK2	16343
	MDS/ MPN/ Leukaemia, MPL	407
	MDS/ MPN/ Leukaemia, PDGFRA rearrangement	338
	MDS/ MPN/ Leukaemia, PDGFRB rearrangement	142
	MDS/ MPN/ Leukaemia/ Lymphoma (gene or locus)	1584
	Medulloblastoma, 2p24	10
	Medullublastoma, 8q24	3
	Melanoma, BRAF V600	1552
	Melanoma, C-MYC	21
	Melanoma, CDKN2A	25
	Melanoma, RREB1, CEP6, MYB, CCND1	34
	Melanoma, rearrangements (various)	1655
	Mesothelioma, BAP1	25
	Mesothelioma, CDKN2A	37
	MGMT methylation	4
	MPN, JAK2 rearr.	2
	Myelodysplastic Syndrome/ Leukaemia	245
	Myeloma	87
	Myeloma FISH Panel	60
	Myeloma, CDKN2C/CKS1B, FGFR3/IGH, MAF/IGH, TP53/D17Z1 rearr.	71
	Myeloma, t(14;16) MAF-IGH	5

Test groups	Tests	No. of tests
	Myeloma, t(14;20) MAFB-IGH	2
	Myeloma, t(4;14), FGFR3-IGH	385
	Myeloma, TP53/NF1	308
	Neuroblastoma, MYCN/AFF3	10
	Neuroblastoma, MYCN/AFF3	4
	Neuroblastoma/ Medulloblastoma	20
	NMYC amplification	41
	Oligodendroglioma, 1p38/19q13	90
	Oligodendroglioma, microsatellite analysis	30
	Oncogene inv CBFB/MYH11 rearr.	135
	Oncogene t(1:9) TCF3/PBX1 rearr.	68
	Pancreatic, KRAS	183
	Rhabdomyosarcoma, alveolar, 13q14	12
	RUNX1 (3'5')	4
	Sarcoma, CDK4	164
	Sarcoma, DDIT3 rearr.	19
	Sarcoma, EWSR1 rearrangements (various)	138
	Sarcoma, FOXO1 rearr.	5
	Sarcoma, FOXO1,MDM2,ALK,KMT2A,TFE3,TP53,DDIT3 rearr.	30
	Sarcoma, IDH1	2
	Sarcoma, IDH2	2
	Sarcoma, MDM2	165
	Sarcoma, PAX3 rearr.	5
	Sarcoma, SS18 rearr.	51
	Sarcoma, synovial, 18q11.2	41
	Sarcoma, miscellaneous rearrangements	136
	Sebaceous adenoma, BRAF V600	3
	Systemic mastocytosis, KIT	15
	Thyroid, BRAF V600	64
	Thyroid, KRAS	4
	Thyroid, NRAS	6
	Leukaemia, confirmatory testing	11
	Miscellaneous oncogene rearrangements	351
Targeted testing *(loci; specific gene variants or regional chromosomal regions)* (Listed by descending order of test frequency)		
	Leukaemia, t(9;22) BCR-ABL1	18715
	MDS/ MPN/ Leukaemia, JAK2	16343
	Lung, EGFR	4203
	Lung cancer, miscellaneous targeted variants	2620
	Breast, ERBB2 (HER2)	2333
	Leukaemia, acute myeloid, FLT3	1846
	Melanoma, rearrangements (various)	1655
	Lymphoma, Clonality (T-Cell Receptor Gene Rearrangement Analysis)	1653
	MDS/ MPN/ Leukaemia/ Lymphoma (gene or locus)	1584
	Colorectal, targeted variants (unspecified)	1569
	MDS/ MPN/ Leukaemia, CALR	1569
	Melanoma, BRAF V600	1552
	Colorectal, KRAS & NRAS	1512

Targeted testing *(loci; specific gene variants or regional chromosomal regions)* (Listed by descending order of test frequency)	
Leukaemia, acute myeloid, t(15;17) PML-RARA	1414
Leukaemia, acute myeloid, t(8;21) RUNX1T1-RUNX1	1304
Lymphoma, Clonality (IGH/ IGK Gene Rearrangement Analysis)	841
Colorectal, BRAF V600	825
Lung, ALK	779
Leukaemia, acute myeloid, NPM1	767
Leukaemia, acute lymphoid, minimal residual disease testing	755
Lymphoma, MYC rearrangement	716
Colorectal/ Endometrial, MLH1 promoter	515
Lymphoma, BCL2 rearrangement	498
Leukaemia, acute myeloid, CBFB rearrangement	487
Leukaemia, acute lymphoid, t(12;21) ETV6-RUNX1	481
Lymphoma, ATM/TP53	474
Lymphoma, BCL6 rearrangement	470
Leukaemia, acute lymphoid, KMT2A (MLL) rearrangement	425
Lymphoma, t(11;14) CCND1-IGH@	414
MDS/ MPN/ Leukaemia, MPL	407
Myeloma, t(4;14), FGFR3-IGH	385
Lymphoma/ Sarcoma D12Z3/MDM2	378
Miscellaneous oncogene rearrangements	351
MDS/ MPN/ Leukaemia, PDGFRA rearrangement	338
Myeloma, TP53/NF1	308
Brain, IDH1	279
Lung, ROS1	264
Leukaemia, acute myeloid, KIT	256
Myelodysplastic Syndrome/ Leukaemia	245
Lymphoma, t(14;18) BCL2-IGH@	244
Leukaemia/ Solid tumour rearrangements (various)	226
Lung, KRAS	218
Cancer, indeterminate (targeted variants)	201
Lymphoma/ MDS/ MPN, RB1/DLEU2/LAMP1	196
Leukaemia, acute myeloid, FLT3 & NPM1	194
Pancreatic, KRAS	183
Leukaemia, acute myeloid, CEBPA	169
Brain, 1p/19q co-deletion	166
Sarcoma, MDM2	165
Sarcoma, CDK4	164
Leukaemia, chronic lymphoid, miscellaneous rearrangements	160
MDS/ MPN/ Leukaemia, PDGFRB rearrangement	142
Sarcoma, EWSR1 rearrangements (various)	138
Sarcoma, miscellaneous rearrangements	136
Oncogene inv CBFB/MYH11 rearr.	135
Colorectal, KRAS	125
Lymphoma, IRF4 rearr.	123
Gastric cancer, ERBB2 (HER2)	114
Lymphoma, MALT1 rearrangement	113
Lymphoma, t(8;14) IGH-MYC	113
Liposarcoma, MDM2	110
Brain, IDH2	107
Lymphoma/ Myeloma, MYC rearr.	96
Haematological disorders, CRLF2, MYC, CCND1, TP53, XY, enumeration probes	90

Targeted testing *(loci; specific gene variants or regional chromosomal regions)* (Listed by descending order of test frequency)	
Oligodendroglioma, 1p38/19q13	90
Myeloma	87
Liposarcoma, 12q15	79
Leukaemia, chronic myeloid, IGHV somatic hypermutation	73
Colorectal, NRAS	72
Myeloma, CDKN2C/CKS1B, FGFR3/IGH, MAF/IGH, TP53/D17Z1 rearr.	71
Oncogene t(1:9) TCF3/PBX1 rearr.	68
Thyroid, BRAF V600	64
Myeloma FISH Panel	60
Leukaemia, acute myeloid, IDH1/ IDH2	56
Brain, EGFR	55
Sarcoma, SS18 rearr.	51
Leukaemia, acute lymphoid, CRLF2; CEP4/10/17; BCR/ABL1; KMT2A; TCF3/PBX1/HLF; ETV6/RUNX1 rearr.	49
Brain, BRAF V600	44
Lymphoma/ Myeloma, t(8;14) MYC-IGH	43
NMYC amplification	41
Sarcoma, synovial, 18q11.2	41
Leukaemia, acute lymphoid, miscellaneous oncogenic mutations	39
MDS, D5S1518E-D5S1976/EGR1/RPS14	37
Mesothelioma, CDKN2A	37
Brain, MGMT	34
Melanoma, RREB1, CEP6, MYB, CCND1	34
Leukaemia/ MDS, D7Z1/KMT2E/MET	33
Brain, BRAF fusion	31
Leukaemia/ MDS MECOM (3'5')	31
Oligodendroglioma, microsatellite analysis	30
Sarcoma, FOXO1,MDM2,ALK,KMT2A,TFE3,TP53,DDIT3 rearr.	30
Leukaemia, CDKN2A/D9Z3	25
Melanoma, CDKN2A	25
Mesothelioma, BAP1	25
Gastrointestinal stromal tumour, KIT	24
Lymphoma, NPM-ALK rearr.	24
Brain, MYC	22
Melanoma, C-MYC	21
Neuroblastoma/ Medulloblastoma	20
Lymphoma, Burkitt, 8q24/14q32)	19
Sarcoma, DDIT3 rearr.	19
Aneurysmal Bone Cyst and Nodular Fasciitis, USP6	17
Leukaemia, CRLF2 rearr.	17
Leukaemia/ Sarcoma FUS rearr.	17
Lymphoma, ALK rearrangement	17
Systemic mastocytosis, KIT	15
Endometrial cancer, BRAF V600	12
IGH hypermutation	12
Leukaemia, D4Z1/D10Z1/D17Z1	12
Rhabdomyosarcoma, alveolar, 13q14	12
Leukaemia, epsinophilic, FGFR3, FIP1L1-CHIC2-PDGFRA, PDGFRB rearr.	11
Leukaemia, confirmatory testing	11
Leukaemia, TLX3 rearr.	10

Targeted testing *(loci; specific gene variants or regional chromosomal regions)* (Listed by descending order of test frequency)	
Liposarcoma, myxoid,12q13 rearr.	10
MDS, PTPRT/20qter	10
Medulloblastoma, 2p24	10
Neuroblastoma, MYCN/AFF3	10
Lymphoma/ Leukaemia, TCL1A rearr.	8
MDS, SCFD2/TET2	8
MDS/ MPN/ Leukaemia, FGFR1 rearr.	8
Gastrointestinal stromal tumour, PDGFRA	7
Glioblastoma, MGMT	7
Lymphoma/ Myeloma, CCND1 rearr.	7
Leukaemia, hairy cell, KIT	6
Thyroid, NRAS	6
Leukaemia, hairy cell, BRAF	5
Leukaemia, RARA (5'3')	5
Lymphoma/ Myeloma, IGH rearr.	5
Myeloma, t(14;16) MAF-IGH	5
Sarcoma, FOXO1 rearr.	5
Sarcoma, PAX3 rearr.	5
Leukaemia, ETV6 rearr.	4
Leukaemia, IKZF1	4
MGMT methylation	4
Neuroblastoma, MYCN/AFF3	4
RUNX1 (3'5')	4
Thyroid, KRAS	4
Langerhans cell histiocytosis, BRAF V600	3
Medullublastoma, 8q24	3
Sebaceous adenoma, BRAF V600	3
Gastric cancer, miscellaneous oncogenic mutations	2
Leukaemia, t(9;11) KMT2A-MLLT3	2
Lymphoma, DUSP22 rearr.	2
Lymphoma, IGK rearr.	2
MPN, JAK2 rearr.	2
Myeloma, t(14;20) MAFB-IGH	2
Sarcoma, IDH1	2
Sarcoma, IDH2	2
Leukaemia, D6Z1/SEC63/MYB	1
Leukaemia, t(4;14), KMT2A-AFF1	1
Lymphoma, IGL rearr.	1
Lymphoma, TP63 rearr.	1
Lymphoma/ Myeloma, t(6;14) CCND3-IGH	1

Targeted Multi-Gene Panels (gene-focussed tests involving 3 or more genes)	
Panel – Myelodysplastic Syndrome/ Leukaemia (51-100 genes)	697
Panel – Myeloid malignancies (51-100 genes)	688
Panel – Colorectal cancer (11-50 genes)	615
Panel – Cancer (11-50 genes)	572
Panel – Lung cancer (11-50 genes)	553
Panel – Lymphoid malignancies (51-100 genes)	466
Panel – Melanoma (11-50 genes)	386
Panel – Lung/ Melanoma/ Colorectal (11-50 genes)	350
Panel – Cancer, indeterminate (101-200 genes)	250

Targeted Multi-Gene Panels (gene-focussed tests involving 3 or more genes)	
Panel – Cancer, comprehensive (101-200 genes)	150
Panel – Lung/ Melanoma/ Colorectal (3-10 genes)	124
Panel – Breast/ Ovarian cancer (11-50 genes)	78
Panel – Cancer, comprehensive (51-100 genes)	50
Panel – Cancer, comprehensive (400+ genes)	50
Panel – Gastric cancer (11-50 genes)	48
Panel – Colorectal cancer (3-10 genes)	39
Panel – Melanoma (3-10 genes)	26
Panel – Lung/ Thyroid Fusion Profile (3-10 genes)	5
Panel – Myeloid malignancies (11-50 genes)	5
Panel – Breast/ Ovarian cancer (3-10 genes)	2

Table 43: Diagnostic biochemical genetic tests (all states and territories)

Test	Testing/ Screening/	Analyte/ Enzyme assay	No. of tests
Acylcarnitine profile (non-neonatal) analysis	Screening (targeted)	Analyte	2522
Amino acids (blood, urine, CSF)	Screening (targeted)	Analyte	15562
Bile acids (urine)	Screening (targeted)	Analyte	98
DNP (urine)	Screening (targeted)	Analyte	24
Glycosaminoglycan screen (urine)	Screening (targeted)	Analyte	11758
Mucopolysaccharides	Screening (targeted)	Analyte	2124
Oligosaccharides	Screening (targeted)	Analyte	117
Polyols, urine	Screening (targeted)	Analyte	23
Purine and pyrimidine (urine)	Screening (targeted)	Analyte	564
Reducing sugars (urine)	Screening (targeted)	Analyte	149
Transferrin analysis for glycosylation defects	Screening (targeted)	Analyte	529
Metabolic screen (Tandem MS) (urine)	Screening (untargeted)	Analyte	3290
Organic acids (urine)	Screening (untargeted)	Analyte	12621
Apolipoprotein C3 (blood)	Testing	Analyte	37
Carnitine	Testing	Analyte	1314
Creatine	Testing	Analyte	77
Creatine & Guadinoacetate (blood, urine)	Testing	Analyte	3
Creatine & Guadinoacetate (urine)	Testing	Analyte	186
Fabry monitoring (Lyso-CTH)	Testing	Analyte	1945
Free fatty acids	Testing	Analyte	490
Glucose tetrasaccharides	Testing	Analyte	77
Glucosidase (dried bloodspot)	Testing	Analyte	378
Guanidinoacetic acid	Testing	Analyte	36
Methylmalonic acid (blood, blood spot, urine)	Testing	Analyte	1154
Orotic acid (urine)	Testing	Analyte	100
Orotic, 3-hydroxyglutaric, glutaric panel (urine)	Testing	Analyte	52
Oxalate (urine)	Testing	Analyte	1157
Plasmalogen	Testing	Analyte	18
Porphyrins (blood and urine)	Testing	Analyte	548
Porphyrins (faeces)	Testing	Analyte	80
Pterins , CSF	Testing	Analyte	93
Pterins, urine	Testing	Analyte	9
Pyruvate	Testing	Analyte	635
Succinyl acetone (urine)	Testing	Analyte	139
Trimethylamine (urine)	Testing	Analyte	57

Test	Testing/ Screening/	Analyte/ Enzyme assay	No. of tests
Very long chain fatty acids/ phytanate/ pristanate	Testing	Analyte	692
3-hydroxybutyric acid	Testing	Analyte	262
7-dehydrocholesterol	Testing	Analyte	315
Alpha-galactosidase (dried bloodspot)	Testing	Enzyme assay	1245
Alpha-1 Antitrypsin	Testing	Enzyme assay	4758
Enzymology – mitochondrial disorders	Testing	Enzyme assay	68
Enzymology – all other inborn errors of metabolism	Testing	Enzyme assay	1380
White cell enzymes	Testing	Enzyme assay	598

Appendix B

Survey instrument
Laboratories were asked to provide the following information:

Type of laboratory (private, public, Catholic/Schedule 3, research/academic)
Options:
- Public
- Private
- Catholic/Schedule 3
- Research/academic

NPAAC Laboratory Category
Options:
- General
- Branch
- Specialised
- Not applicable (not NPAAC/pathology lab)

Laboratory department
Options:
- Anatomical Pathology
- Chemical Pathology
- Endocrinology
- Genetic Pathology
- Haematology
- Immunopathology
- Research
- Other, please specify

NATA accredited for genetic testing?
Options:
- Already NATA accredited
- An 'Applicant Laboratory' for NATA accreditation
- Not currently NATA accredited

NATA accredited for Massively Parallel Sequencing?
Options:
- Yes (under 2017 NPAAC requirements)
- Yes (under earlier NPAAC requirements)
- No

If not accredited for MPS, please indicate the reason:
Options:
- Not applicable
- Overcoming challenges associated with the 2017 NPAAC requirements

Referring Clinicians
List the number of genetic/ genomic test referrals coming from the following categories of clinicians from 1 July 2016 to 30 Jun 2017

Options:

- Clinical Geneticists
- General Practitioners
- Obstetricians/ Fertility/ Fetal Medicine Specialists
- Paediatricians
- Oncologists
- Endocrinologists
- Cardiologists
- Neurologists
- Pathologists
- Anatomical Pathologists (including Forensic, Perinatal and Paediatric)
- General Pathologists
- Chemical Pathologists
- Haematologists
- Immunopathologists
- Other medical specialists or referrers – specify:
- Other referral pathways (e.g. newborn bloodspot screening, Ashkenazi screening program) – specify:

Patient Numbers
Total number of patients for whom test results for genetic/ genomic testing were issued

Sample Volumes
No. received for genetic/ genomic testing during the survey period?
No. inadequate (repeat sample required)?
No. inappropriate clinical requests?
No. received for storage only?
No. referred out (options: international/ interstate/ intrastate) for analysis and reporting?
No. referred out (options: international/ interstate/ intrastate) for analysis (wet work) only?
No. external quality assurance samples (e.g. QAP, sample exchange)?
No. familial positive control samples?

Staffing
No. full-time equivalents, or portions thereof, of staff time focussed on genetic/ genomic testing:

- FRCPA (specify discipline); trainees
- FFSc (specify discipline and pathway (options – founding, examination, research)
- FHGSA/ MHGSA (scientists)
- Other fellowship/ postgraduate qualifications (e.g. FAACB, PhD or overseas Fellowship).
- Clinical Bioinformatician *(trained in both (a) computer algorithms and statistical methods used to analyse data generated by assays used in clinical testing, (b) software engineering practices associated with producing software for use in clinical environments)*

- Informatician (Pathology or Health Informatics)/ IT staff/ Computer Scientist (trained in systems or associated computing technology that stores and manages health data)
- Technician/ Assistant
- Other Medical Staff: Clinical Geneticist (FRACP, FHGSA), Other – specify:
- Genetic Counsellor (Certified, FHGSA or equivalent; Associate)
- Clerical Officer

General Laboratory Information Management System (LIMS)

Request/ Sample registration:

- Laboratory workbooks
- Local electronic record/ database (laboratory hard drive)
- Local electronic record/ database (laboratory/ hospital server)
- LIMS
- Local system and LIMS

Workflow and sample tracking:
Laboratory workbooks

- Local electronic record/ database (laboratory hard drive)
- Local electronic record/ database (laboratory/ hospital server)
- LIMS
- Local system and LIMS

Report storage:
Hardcopy storage

- Local electronic record/ database (laboratory hard drive)
- Local electronic record/ database (laboratory/ hospital server)
- LIMS

Genetic/ Genomic Data Storage

Type of data storage infrastructure used 2016/17 financial year:

- Local hard drive
- Local portable storage device(s)
- Local server in lab
- Hospital server
- External data warehouse
- Cloud storage
- Multiple, please specify
- Other, please specify

Laboratory satisfied with current data storage facility?

- Yes
- No

Details of locally identified variants stored in searchable database(s):

- Yes - for all variants
- Yes - for some variants
- No
- If yes, indicate arrangement:
    - Commercial
    - In-house
    - Both commercial & in-house used

Details of locally identified variants submitted to external database(s) (e.g. DECIPHER, ClinVar, LOVD)?

- Yes - for all variants
- Yes - for some variants
- No

Test Requests
Laboratories asked to list tests using the following classification/ nomenclature:

"Genome scale" testing – e.g. karyotyping, microarray analysis, "untargeted" massively parallel sequencing or DNA methylation analysis:

- Chromosomal karyotyping
- Chromosomal microarray analysis
- Whole Genome Sequencing
- Whole Exome Sequencing
- "Untargeted" disease gene panel (e.g. TruSight One)
- Genome-scale DNA methylation analysis

Targeted Loci/ Regional Chromosome, Epigenetic Tests

- Aneuploidy Screening (rapid or non-invasive prenatal)
- Linkage Studies (family linkage, "trio", etc.)
- Maternal Cell Contamination
- Methylation
- Other (specify)

Tests for conditions involving 1 or 2 genes/ imprinting centres
Examples:

- Achondroplasia (FGFR3)
- Charcot-Marie-Tooth Type 1A (PMP22 duplication)
- Cystic Fibrosis (CFTR)
- Duchenne/Becker Muscular Dystrophy (DMD gene)
- Factor V Leiden (F5)
- Haemochromatosis (HFE genotyping)
- Myotonic Dystrophy
- Prothrombin (F2)
- Rett Syndrome (MECP2)
- Thiopurine S-methyltransferase (TPMT)
- Other (specify)

Targeted multi-gene panels (gene-focussed tests involving 3 or more genes)
Examples:

- Cardiomyopathy
- Breast and Ovarian
- Epilepsy
- Myopathy
- Ashkenazi Jewish Disease Genes
- Disorders of Sexual Development
- Other (specify)

Test Target/ Scope

Laboratories asked to categorise the targets and scope of each listed test using the following selection options:

Biochemical:

Pregnancy screening:

- Maternal first trimester screening (blood chemistry for CFTS)
- Maternal second trimester screening (2TMSS)

Newborn bloodspot screening

Diagnostic assessment:

- Acyl carnitine profile (non-neonatal) analysis
- Amino acids (blood, urine, CSF)
- Carnitine
- Enzymology - mitochondrial disorders
- Enzymology - all other inborn errors of metabolism
- Glycosaminoglycan screen (urine)
- Mucopolysaccharide analysis (urine)
- Methylmalonic acid (blood, blood spot, urine)
- Mucopolysaccharides
- Organic acids (urine)
- Porphyrins (blood and urine)
- Purine and pyrimidine (urine)
- Transferrin analysis for glycosylation defects
- Steroid hormones (excl. 7DHC – see below)
- Very long chain fatty acids/ phytanate/ pristanate
- 7-dehydrocholesterol
- Other (enter text using Other as prefix)

Cyto-molecular:

Specified variant(s):

- Single variant (small nucleotide level)
- Multiple targeted variants in a single gene (small nucleotide level)
- Multiple targeted variants in multiple genes (small nucleotide level)
- Targeted deletion(s)/ duplication(s)/ dosage analysis
- Targeted rearrangement analysis
- Gene amplification analysis
- Genome mutability analysis (e.g. MSI)
- Targeted methylation analysis
- Other (specify)

Unspecified variant(s):

- Single gene
- Two genes
- 3 – 10 genes
- 11 – 50 genes
- 51 – 100 genes

- 101 – 200 genes
- 201 – 300 genes
- 301 – 400 genes
- 400+ genes
- Whole Exome Analysis
- Whole Genome Analysis
- All Chromosomes (including karyotype and microarray)
- Other (specify)

Test Methods
Laboratories were asked to provide details of test methods using the following selection options:
Cytogenetic

- Karyotype– banded analysis
- FISH
- Other (specify)

Molecular

- Microarray
- Sanger sequencing
- Single Nucleotide Primer Extension (minisequencing)
- Massively Parallel Sequencing (MPS)
- MALDI-TOF
- Southern Blot analysis
- Other (specify)

Clinical Referral Categories
Laboratories were asked to indicate test numbers for each of the following clinical referral categories:

Diagnostic

- Constitutional - symptomatic index cases patient
- Cancer – tumour/ blood/ bone marrow samples
- Family segregation analysis (to assist variant classification)
- Familial cascade testing of a known pathogenic variant (including presymptomatic/ predictive; excluding carrier testing for recessive/ X-linked disorders)
- Recessive/ X-linked carrier testing (high prior risk)

Therapy selection/ monitoring

- Tumour sample genotyping
- Minimal residual disease/ transplant monitoring
- Pharmacogenomic testing (constitutional)

Prenatal

- Testing of fetal tissues (amnio, CVS, fetal blood, other fetal tissues)
- Maternal blood (fetal DNA aneuploidy screening)
- Maternal blood (fetal DNA Rhesus screening)

Pre-implantation genetic testing

- Aneuploidy screening
- High risk monogenic disease testing

Population screening

- Newborn bloodspot screening
- Genetic disease detection (population risk
- Recessive mutation carrier screening (population risk)

Reporting Times
For each clinical referral category, laboratories were asked to provide reporting times in calendar days (50th and 90th centiles)

State of Origin of Test Request
For each test category, laboratories were asked to enter the number of cases originating from each state and territory

Funding Sources
For each test category, laboratories were asked to indicate the sources of payment for genetic/ genomic tests requested for patients from all states and territories.

Options:

- Federal (Medicare)
- State
- Grant/ Contract
- Patient
- Other

International Test Requests

Outgoing
For samples sent overseas, list the top 10 test request categories and, for each, the numbers of tests referred.

Incoming
Total numbers of tests performed on samples received from other countries.

Covering Letter

The Royal College of Pathologists of Australasia
ABN 52 000 173 231

Durham Hall 207 Albion Street Surry Hills NSW 2010 Australia
Telephone 61 2 8356 5858 Facsimile 61 2 8356 5828

RCPA
The Royal College of Pathologists of Australasia

Updated Health Genetics and Genomics Survey

The National Health Genomics Policy Framework (the Framework), endorsed by the Council of Australian Governments Health Council in November 2017, has been establised to better integrate genomics into the Australian health system. Health genomics is a rapidly changing field and information about the current testing environment is essential for good decision making by policy makers at all levels of Government.

As a first step, to support implementation of the Framework, the Australian Health Ministers' Advisory Council (AHMAC) has commissioned a national genetic and genomic testing and activity stocktake. The stocktake data is expected to form a baseline of genetic and genomic testing and activities:

- to support the Frameworks's Implementation Plan, which outlines priority activities for implementation, policies for development and the roles and responsibilities of governments and other stakeholders;
- to provide a reliable evidence base for decision makers considering the implications of policies, including models for funding and workforce strategies; and
- to support ongoing monitoring, reporting and evaluation of the Framework.

Previous surveys of genetics' laboratories by the Royal College of Pathologists of Australasia (RCPA) in 2006 and 2011 documented the utilisation of genetic testing for medical purposes. The 2012 report indicated the volumes, types and purposes of genetics testing. Importantly it indicated the range of funding sources, variations across Australian States and analysed the changes occurring in the intervening five years.

This stocktake will provide up-to-date data on the availability and volume of genetics and genomics testing in Australia to understand how services are currently being used. This snapshot will provide a baseline of activity for the Framework and an indication of change since the last survey took place, which will inform future workforce requirements and modelling for future best practice patient service provision.

The RCPA has been contracted to undertake the stocktake of genetic and genomic testing in Australia. A Steering Committee established from pathologists and scientists in the disciplines of Genetic Pathology, Anatomical Pathology, Haematology and Immunopathology and Genomic Research is providing guidance and oversight of the project on behalf of the RCPA. Steering Committee members are representative of the Australian Genomics Health Alliance and the Human Genetics Society of Australasia and have the required somatic and germline knowledge of and expertise in the Australian genomic testing environment. A Technical Working Group of the National Health Genomics Policy Framework Reference Group has provided additional guidance and oversight of the test stocktake project on behalf of the Commonwealth and State and Territory Governments.

All Australian laboratories involved in human genetic and genomic testing are invited to participate to provide information on the types and volumes of testing performed during the 2016-2017 financial year, **1 Jul 2016 to 30 Jun 2017**.

As was instituted in the previous survey, the privacy of all data collected will be respected to ensure strict confidentiality, as outlined in the Confidentiality Agreement.

Included are:

1. Health Genomics survey laboratory questions – a spreadsheet for your completion
2. Health Genomics survey test questions – a spreadsheet for your completion
3. Health Genomics survey Guide for participants – to assist with completing the survey
4. Health Genomics survey Confidentiality statement – a form for your signature

The RCPA welcomes the opportunity to identify the scale and recent changes in health genetic and genomic testing. The outcomes of this survey will be relevant to all of us engaged in Pathology and will influence the quality of testing available for all Australians.

Any queries regarding the survey or privacy of data should be directed to the Project Manager, Vanessa White at healthgenomics@rcpa.edu.au or Project Leads Prof David Ravine / Dr Sarah Nickerson on (08) 6383 4234.

Health Genetics and Genomics Survey 2017

CONFIDENTIALITY AGREEMENT

I, **Vanessa White**, being the Project Manager, hereby agree and confirm that

1. All information provided by any participating laboratory to me in my capacity as Project Manager will remain confidential at all times, by which is meant:
   - raw identified laboratory data will only be seen by the Project Team: Prof David Ravine, Dr Sarah Nickerson, Ms Vanessa White and a data analyst (to be determined).
   - the Steering Committee, Technical Working Group and the Commonwealth Government will only have access to de-identified consolidated data and as such will not be privy to raw identifed laboratory data.

2. During the conduct of the Project, or at any time afterwards, the Project will not use confidential data except for the express purpose for which it was supplied.

3. During the conduct of the Project, or at any time afterwards, the Project will not disclose, in any manner whatsoever, the cofidential information supplied by any laboratory. Information will only be released in de-identified aggregated form.

4. Aggregation will be at both National and State levels. State-level aggregation will be determined by the originating source of each test request.

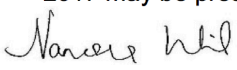
5. Confidential information includes data supplied by the participating laboratory and knowledge gained subsequent to collation and analysis of this data that would identify individual laboratories.

6. All laboratories will be issued with a unique identification code. All data should be submitted by participating laboratories using this code. The only persons with access to the identification of the individual laboratories will be the Project Team.

7. All reasonable steps will be taken to maintain the confidentiality and security of all identifiable information.

8. The raw identifed laboratory data supplied by participating laboratories will be retained securely after analysis and reporting by the RCPA. The data will be used for the purposes of validation and to build a longitudinal data set in the event that the survey is repeated. The consolidated de-identified data will be held by the RCPA.

9. Consolidated de-identified data collected in the course of Health Genetics and Genomics Project 2017 may be presented at relevant scientific and Government meetings.



Vanessa White **Date: 26 February 2018**

Agreed on behalf of the participating laboratory: _____

_____ **Date:** _____
Signature

_____ **Date:** _____
Name

Please return ***Scan & email to***

healthgenomics@rcpa.edu.au

Confidentiality Deed

Drawn up later in response to concerns from the private laboratory sector.

Confidentiality Deed

Dated

Parties	Pathology Laboratory ABN xx xxx xxx xxx of Address State Postcode (**Pathology Laboratory**)	**The Royal College of Pathologists of Australasia** ABN 52 000 173 231 of 207 Albion Street, Surry Hills NSW 2010 (**RCPA**)

Introduction

A RCPA wishes to receive Confidential Information from [Pathology Laboratory] in connection with the Project.

B [Pathology Laboratory] has agreed to give RCPA access to, and the right to use, the Confidential Information on the terms set out in this Deed.

It is agreed

1 Definitions and interpretation

1.1 **Definitions**

(1) **Approved Purpose** means use only in relation to the Project;

(2) **Confidential Information** means all information supplied by [Pathology Laboratory] to RCPA in relation to the Project;

(3) **Disclose** means to make known or to reveal by any means, and includes enabling a person to obtain access;

(4) **Deed** means this document;

(5) **Project** means the Health Genetics and Genomics Survey 2017 being conducted by RCPA pursuant to the Contract for Services (Reference ID: 1000067436) between the Commonwealth Department of Health and RCPA dated 20 December 2017;

(6) **Project Manager** means Ms Vanessa White;

(7) **Project Team** means the project team established by RCPA to manage the Project on its behalf, comprising Prof David Ravine, Dr Sarah Nickerson, the Project Manager and a data analyst to be retained by RCPA in relation to the Project; and

(8) **Representative** of a person means:

(a) a related body corporate of the person;

(b) an employee, consultant, officer, agent, auditor, or partner of the person or its related body corporate;

(c) a financial, tax, accounting, legal or other expert adviser of the person or its related body corporate; or

(d) any other person with the prior written consent of [Pathology Laboratory].

1.2 **Interpretation**

(1) Reference to:

(a) the singular includes the plural and the plural includes the singular;

(b) a person includes a body corporate;

(c) a party includes the party's executors, administrators, successors and permitted assigns; and

(d) a statute, regulation, code or other law or a provision of any of them includes:

(i) any amendment or replacement of it; and

(ii) another regulation or other statutory instrument made under it, or made under it as amended or replaced.

(2) "Including" and similar expressions are not words of limitation.

(3) Where a word or expression is given a particular meaning, other parts of speech and grammatical forms of that word or expression have a corresponding meaning when used in this Deed.

(4) Headings are for convenience only and do not form part of this Deed or affect its interpretation.

(5) A provision of this Deed must not be construed to the disadvantage of a party merely because that party was responsible for the preparation of this Deed or the inclusion of the provision in this Deed.

2 Consideration

RCPA gives the undertakings in this Deed in consideration of [Pathology Laboratory] agreeing to Disclose or procure its Representatives to Disclose the Confidential Information in accordance with this Deed.

3 Confidentiality obligations

RCPA agrees that:

(1) any raw identified laboratory data supplied by [Pathology Laboratory] in relation to the Project will only be seen by the Project Team, and that such data must not be disclosed by the Project Team;

(2) subject to paragraphs (9) and (11) below, during the conduct of the Project, and at any time afterwards, RCPA must not use the Confidential Information except for the Approved Purpose;

(3) during the conduct of the Project, and at any time afterwards, RCPA must not Disclose the Confidential Information except in a de-identified aggregated form as part of the results of the Project;

(4) the release of Confidential Information in a de-identified aggregated form will be done at National and State levels only and the State-level aggregation will be determined by the originating source of each test request;

(5) [Pathology Laboratory] will be issued with a unique identification code and that the Project Team must direct [Pathology Laboratory to submit all Confidential Information using this code;

(6) the only persons with access to [Pathology Laboratory] identification code will be the Project Team;

(7) all reasonable steps will be taken by RCPA to maintain the confidentiality and security of all identifiable information;

(8) any raw identified Confidential Information supplied by [Pathology Laboratory] must be retained securely by RCPA after analysis and reporting;

(9) any raw identified Confidential Information must only be used by the Project Team for the Approved Purpose and for the purposes of validation and to build a longitudinal data set in the event that a survey, similar to the Project, is conducted in the future;

(10) the consolidated de-identified Confidential Information must be retained securely by RCPA following completion of the Project; and

(11) the consolidated de-identified Confidential Information collected in the course of the Project may be presented at relevant scientific and Government meetings and by signing this Deed [Pathology Laboratory] consents to such use.

4 General

(1) Each party must pay its own costs and outlays connected with the negotiation, preparation and execution of this Deed.

(2) This Deed may be executed in any number of counterparts. Each counterpart is an original but the counterparts together are one and the same Deed.

(3) The law of New South Wales governs this Deed. The parties submit to the non-exclusive jurisdiction of the courts of New South Wales and of the Commonwealth of Australia.

Executed as a deed and delivered on the date shown on the first page.

Executed by [Pathology Laboratory] ABN xx xxx xxx xxx in accordance with section 127 of the *Corporations Act 2001*:

Director/company secretary	Director
Name of director/company secretary (BLOCK LETTERS)	Name of director (BLOCK LETTERS)

Executed by **The Royal College of Pathologists of Australasia** ABN 52 000 173 231 in accordance with section 127 of the *Corporations Act 2001*:

Director/company secretary	Director
Name of director/company secretary (BLOCK LETTERS)	Name of director (BLOCK LETTERS)

Survey Guide for participants

Thank you in advance for agreeing to complete this survey. We recognise the many demands on your time and very much appreciate your involvement. The purpose of the survey is to provide an accurate stocktake of the range and volumes of genetic/ genomic tests completed across Australia over the past financial year.
The scope of the survey is to define:

- The full range of genetic, genomic and biochemical tests (for both heritable and somatic variants, including cancer) being offered across Australia
- The proportion of tests completed on local (same State) and remote (Interstate and International) samples
- The type/ volume of tests sent to and received from International laboratories
- The volume and proportions of tests within each of the major clinical referral categories
- Test request rates (per 100,000 people) for each State-based patient group (restricted to the groups of tests where state-by-state comparisons do not provide insights into the test volumes of any specific laboratory)
- The proportion of samples that are not tested because of sample quality issues or inappropriate clinical requests
- Funding sources and the proportion of funding derived from each source
- Current staffing levels in genetic/ genomic testing laboratories

This de-identified information will inform the implementation of the first National Health Genomics Policy Framework (the Framework). Findings from the stocktake will be considered by Commonwealth, State and Territory Departments of Health to better understand the current scope and volume of genetic and genomic tests completed for Australian patients.
We know that there are sensitivities regarding the collection and use of this information. Your laboratory's raw identified data will only be seen by the Project Team members*.
Only **de-identified consolidated data** (as referred to in the Confidentiality form) will be made available to the Commonwealth, State and Territory Departments of Health, Project Committees, RCPA Executive, Fellows, Committees, or other professional bodies.
We are approaching all medical testing and research labs known to have provided human genetic, genomic and biochemical genetic tests for medical purposes. If you are working in a multi-lab organisation, please check with colleagues to ensure that you are neither duplicating nor omitting survey data. Some organisations may choose to complete the surveys centrally. However, a survey should be submitted from **each** laboratory contributing data specific to its department and location that corresponds to its unique identifier.

Scope of survey

The following information is sought for **all cytogenetic, molecular genetic, genomic and biochemical tests requested for clinical purposes** *(constitutional and cancer-related testing)*

- All cytogenetic, molecular genetic, genomic and biochemical genetic tests (including newborn and maternal serum screening) that were completed during the 2016-2017 financial year *(**1 July 2016 to 30 June 2017)***
- Tests performed in Australian laboratories on local state and interstate samples
- Tests performed on overseas referred samples
- Numbers of tests referred to overseas laboratories

*The survey **excludes**:*

- *Medical testing of non-human genes (e.g. microbial genetic testing).*

- *Non-medical testing of human genes (e.g. paternity testing, forensic testing)*

Please note: To avoid "double-counting" the laboratory **reporting** the test results should supply details about the completed number of tests.

- Tests completed on samples referred from **intrastate** or **interstate** laboratories should be counted by the receiving (i.e. testing) lab; the sending lab should not report these test numbers.
- Samples tested locally **then** subsequently sent to another Australian lab (intra- and interstate) for further testing, should be counted twice; once for the original test, and again by the recipient laboratory that completed the follow-up investigation.
- For test request referrals forwarded overseas for analysis, only limited information is being sought for your laboratory's ten most commonly referred test request categories (numbers of sample referred over the 12-month period).
- For family segregation analysis (linkage analysis or studies directed towards resolving uncertainty about variant classification), each family member included in the analysis should be counted as a **separate** testing event even though the results may be combined with those from other relatives.

Survey tool
The survey is in the form of two Excel spreadsheets; Laboratory Questions and Test Questions, and a Confidentiality Statement. Your laboratory has been provided with a secure ShareFile logon and your organisation has been assigned a **unique identifier.**
After data entry has been completed, please save the files, maintaining the assigned name of the files, and upload to the Submission folder in your ShareFile account. Please also upload the signed confidentiality agreement and retain a copy for your records. Once complete, please send an email to healthgenomics@rcpa.edu.au confirming that your Submission has been finalised and uploaded to ShareFile.

Health Genetics and Genomics survey 2017: Laboratory questions

This spreadsheet consists of general questions about the total number of request referrals and completed tests and staff resources in your laboratory. Please complete by selecting an option from the drop-down lists provided, or entering an appropriate value or free text in the boxes provided. A data check box is provided at the top right of the page as an aid to indicate any missing data.

1. Health Genetics and Genomics survey 2017: Test questions

This spreadsheet is designed to collect more detailed information about tests performed by your laboratory. The spreadsheet has three tabs – Constitutional CytoMolecular; Cancer CytoMolecular, and Biochemical Genetics. Select the tab(s) relevant for your laboratory's test repertoire.

Constitutional CytoMolecular; Cancer CytoMolecular

For each Test Request entry, select the name of the disease/ gene test(s) from the drop-down list. If a desired Test Request option is not listed, please enter "Other – Test Name" with free text. For each row entry, there are two subsequent columns with drop-down lists of options that will allow the tests to be further categorised for subsequent meaningful analysis.

The first few highlighted rows of the sheet contain sample data to demonstrate how to complete the survey. For each test provide the following:

Test Request (Column C)

(Examples: Cystic Fibrosis (CFTR); Panel – Aortopathy; Chromosomal Karyotyping; Chimerism Analysis)

- Please list **all tests offered** by your laboratory, **even if none were performed** during the survey period.
- Please list each test on a separate row, wherever possible selecting an option from the drop-down list (click on the drop-down arrow). Please note, the number of listed options is reduced compared with the drop-down list for the 2011 survey.

Test Target/ Scope (Column D)

(Examples: multiple targeted variants in a single gene (small nucleotide level); targeted rearrangement analysis; genome mutability analysis (e.g. MSI); untargeted variants in 11-50 genes; whole exome analysis; all chromosomes)

For each test entry, select the most appropriate descriptor from the drop-down list.

Test Method (Column E)

(Examples: Karyotype– banded analysis; Chromosomal breakage studies; Microarray; Sanger sequencing and MLPA; Massively Parallel Sequencing (MPS); MALDI-TOF; Southern Blot analysis)

For each Test Request item, enter the most appropriate method category. These broad categories will aid the task of summarising the wide range of testing methods that are now in use.

Clinical Referral Categories (Columns F-U)

(Examples: Diagnostic assessment: Constitutional – symptomatic index case, Somatic – tumour/ blood/ bone marrow samples; Therapy selection or monitoring: Tumour sample genotyping, Minimal Residual Disease; Prenatal: Testing of Fetal Tissues; Maternal Blood – fetal DNA aneuploidy screening)

To comply with the Department of Health's requirement for information about test clinical indications, it has been necessary to increase the number of clinical referral categories. Individual tests offered by most laboratories will be for a limited number of clinical referral categories. Laboratories need only enter data for their own relevant clinical referral categories. Empty cells in the "Clinical Referral Categories" columns are not flagged as "incomplete" by the embedded data entry check.

Total tests performed (no.) (Column V)

The numbers of tests included for each clinical referral category are tallied in column V, headed "Total tests performed (no.)". Please check that the total number tallies with your laboratory's records.

Reporting (Turnaround) Times (Columns W-BB)

The single reporting (turnaround) time column from the 2011 survey has been expanded to reflect the different clinical referral categories and enable more meaningful data collection. For each referral category that applies, please enter in **calendar days** the **median (50th centile)** and **90th centile** (the number of days when 90% of reports have been issued). The number of days should be calculated from the time of sample receipt (rather than sample collection).

Tests on State/ Interstate samples (no.) (Columns BC-BI)

Please enter the **number** undertaken for every listed test from each Australian State or Territory during the survey period.

Funding source State samples (Columns BJ-BO)

Please estimate the **percentage** of State sample test costs that came from the various funding categories. The total must be 100% (if any tests in that category were performed) or 0% (if no tests in that category were performed) in the survey period.

- **Federal** refers to any form of Federal (Commonwealth) Government funding, including Medicare and Veteran's Affairs.
- **State** refers to State Government funding, irrespective of recharge arrangements between health units.
- **Grants/ Contracts** refers to research grants, government and commercial contracts
- **Patient** refers to testing paid for by patients and their families.
- **Other** refers to any other major funding source. Examples might include charitable, community or individual donations of funds intended to pay for testing of persons other than testing on the donor.

Funding source Interstate samples (Columns BP-BV)

Please estimate the **percentage** of Interstate sample test costs that came from the listed funding sources. The total must be 100% (if any tests in that category were performed) or 0% (if no tests in that category were performed) in the survey period.

- **Referring service** refers to charges billed to the referring service (lab or clinical service).
- **No charge** refers to tests for which no cost was recovered.
- **Federal, Grants, Patient** and **Other** are defined as above for **State** samples.

Tests on International samples (no.) (Column BW)

Please enter the **number** undertaken for each listed test on samples received from International locations during the survey period.

- Where the test was offered but **no testing** was undertaken, please enter **0**. Do not leave blank.

Other information (Column CJ)

Use free text to contribute any further information about the test that is not captured in the other data fields.

Data Check (Column CK)

Where there is an entry in every column, the **Data Check** cell for each test will be green. Where one or more is blank, the **Data Check** cell will be red to indicate that there are missing data. Where purpose and funding percentages do not add up to 100% or 0%, the **Data Check** will be red.

2. Confidentiality statement

This document is a signed record of the Project Manager's commitment to maintain the privacy and confidentiality of the survey data. Please sign to indicate your acceptance of this commitment, submit with the completed spreadsheets and retain a copy for your reference.

Thank you again for your contribution to this valuable stocktake. For further information or clarification, please contact the Project Team at the email address below.

Vanessa White

Project Manager

[healthgenomics@rcpa.edu.au]

*** Project Team Members**

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2. Dr Sarah Nickerson sarah.nickerson@health.wa.gov.au
3. Ms Vanessa White vanessaw@rcpa.edu.au
4. A/Prof Brett Lidbury

References:

1. National Health Genomics Policy Framework (2017): Commonwealth of Australia; ISBN: 978-1-76007-327-5.
2. NPAAC Requirements for the Supervision of Pathology Laboratories (2007 Edition): Commonwealth of Australia; ISBN: 1-74186-509-3.
3. Australian Government Department of Human Services. Medicare Australia Statistics: Medicare Item Reports [Internet]. [Cited 10 Sep 2018]. Available from: http://medicarestatistics.humanservices.gov.au/statistics/mbs_item.jsp