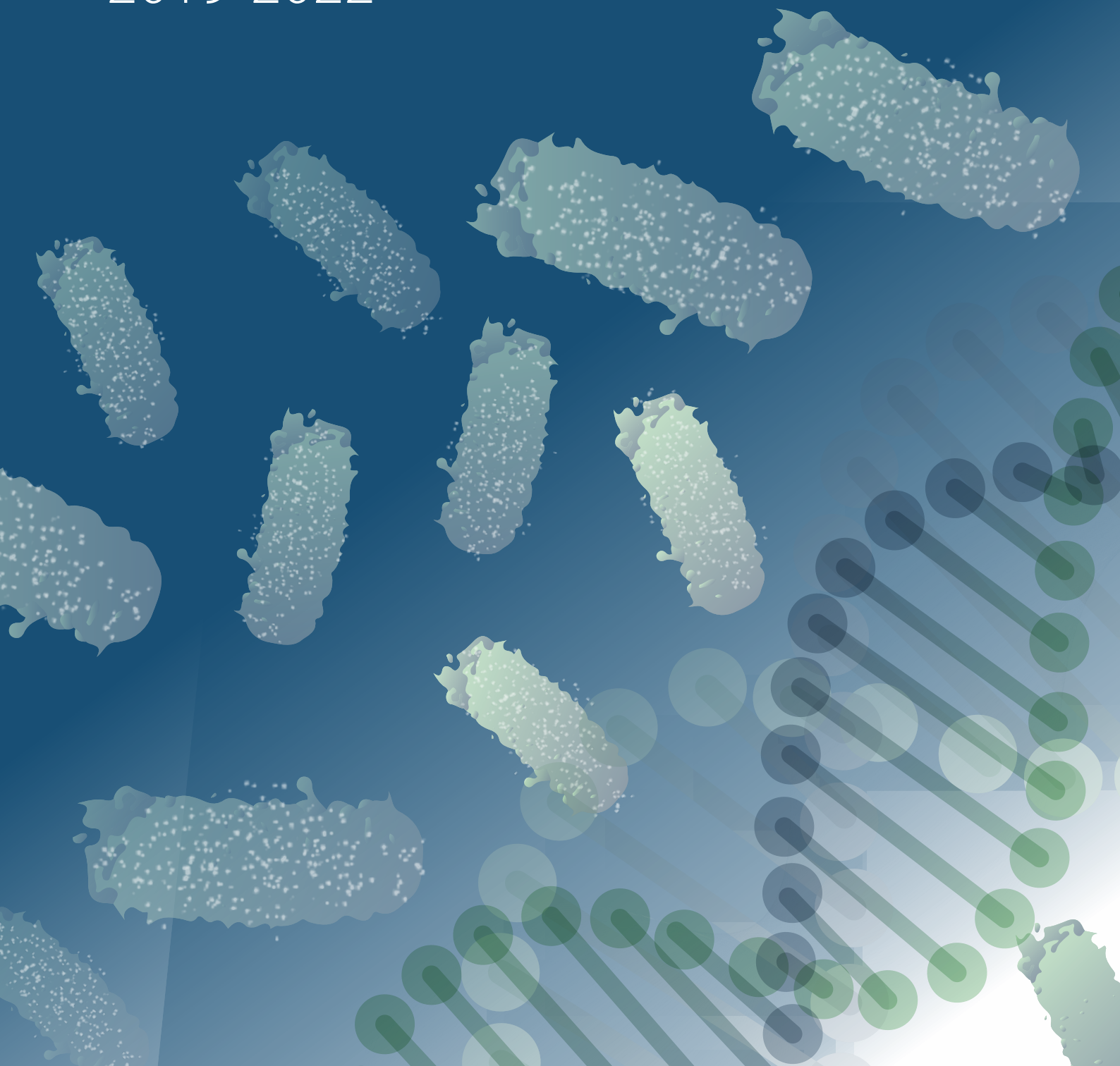
Australian Government
Department of Health

National Microbial Genomics Framework

2019-2022



National Microbial Genomics Framework 2019-2022

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Foreword

The National Microbial Genomics Framework 2019-2022, endorsed by the Australian Health Protection Principal Committee, presents a collaborative commitment to integrating microbial genomics into the Australian laboratory and public health systems.

Our vision is to protect the health of all Australians from communicable disease and biological agent threats by harnessing microbial genomics, genomic knowledge and advanced sequencing technology in a consistent, efficient and effective way in order to improve public health surveillance and response.

Communicable disease control remains a significant public health priority in Australia and internationally. The challenges facing Australia are diverse and include foodborne diseases, emerging antimicrobial resistant organisms and vector-borne diseases. We are now seeing opportunities for microbial genomics to contribute to the rapid identification of clusters of disease transmission, detection of emerging pathogens, and high-resolution typing data for communicable diseases surveillance and bio-threat detection. Globally, the use of microbial genomic technology is rapidly increasing, driven by accessible and advanced sequencing technologies and efficient bioinformatics data analysis.

The first Australian National Microbial Genomics Framework provides a consistent national view for integrating microbial genomics in the Australian public health system and seeks to highlight key policy issues and challenges. It highlights that a skilled health workforce, a robust technological infrastructure and a sustainable funding model are critical to support and maximise the benefits of microbial genomics technology in Australia.

Through close consultation with the states and territories, the framework recognises that strong collaborative relationships between national, state and territory governments, medical laboratory professionals, researchers and health professionals are critical in supporting implementation of microbial genomics in a way that is safe, ethical and equitable.

The strategic priorities within this framework are designed to drive national effort on agreed priorities and will evolve and adapt to the rapidly advancing sequencing and data analysis technologies and practices. It is important to stay at the forefront of this innovative public health practice to ensure that Australia is equipped to monitor, identify, control and respond to, disease outbreaks and bio-threats into the future.

I would like to acknowledge those who have contributed to the development of this framework—notably, the Office of Health Protection, the joint Public Health Laboratory Network and Communicable Diseases Network Australia Project Reference Group on Microbial Genomics, and the Communicable Diseases Genomics Network. Your generosity in sharing your expert knowledge, enthusiasm and commitment to public health has been invaluable to establishing the future direction of microbial genomics in Australia.

Professor Brendan Murphy
Australian Government Chief Medical Officer

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Glossary of key technical terms

For the purposes of the National Microbial Genomics Framework 2019-2022, key terms are defined as follows.

Bioinformatics	The use of algorithms and software to analyse sequencing data.
DNA	Deoxyribonucleic acid—a self-replicating material which is present in nearly all living organisms as the main constituent of chromosomes. It is the carrier of genetic information.
Efficiency	A measure of whether health care resources are being used to get the best value for money. Includes technical, productive and allocative efficiency.
Gene	The basic physical and functional unit of heredity. Genes, which are made up of DNA, act as instructions to make molecules called proteins.
Genome	The complete set of genetic information in an organism.
Genomics	The application of genome-based knowledge through the study of genes and other genetic information, their functions and interrelationships for the benefit of human health.
Genomic data	Refers to data produced from DNA sequencing of a genome.
Genomic knowledge	Includes information about the interpretation of genomic data and the implications of these findings, as well as relevant non-genomic clinical information.
Genomic services	Genome sequencing and analysis available for research, screening and diagnostic purposes.
Genomic surveillance	Involves the monitoring of pathogen evolution, transmission and dissemination, including distribution and evolution of antimicrobial resistance determinants and lineages. This type of surveillance involves applying the principles of evolutionary biology to determine the relatedness of pathogens.
Genomic testing	Involves the analysis of hundreds or even thousands of genes from a pathogen simultaneously using sophisticated computer-based algorithms.
Governance	The structures and processes by which the health system is regulated, directed and controlled. It includes the obligations of stewardship—ensuring that the system is well sustained for the future as well as serving the needs of the present.

Metadata	A set of data that describes and gives information about other data.
Microbial genomics	A scientific discipline that uses the application of genome-based knowledge to study and analyse the genome, functions and entire hereditary information of microbes or microorganisms—bacteria, viruses or fungi.
One health	An approach to designing and implementing programs, policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes.
Pathogen	A microorganism that can cause disease.
RNA	Ribonucleic acid—a nucleic acid present in all living cells. Its principal role is to act as a messenger carrying instructions from DNA to initiate and control the synthesis of proteins, although in some viruses RNA rather than DNA carries the genetic information.
Whole genome sequencing	A laboratory process to determine the complete DNA sequence of an organism's genome.

Acronyms and abbreviations

ABLN	Australian (Counter) Bioterrorism Laboratory Network
AHPPC	Australian Health Protection Principal Committee
AMR	Antimicrobial resistance
CDC	United States Centers for Disease Control and Prevention
CDGN	Communicable Diseases Genomics Network
CDNA	Communicable Diseases Network Australia
DNA	Deoxyribonucleic acid
FDA	United States Food and Drug Administration
Health	Australian Government Department of Health
MDU PHL	Microbiological Diagnostic Unit Public Health Laboratory
NATA	National Association of Testing Authorities
NPAAC	National Pathology Accreditation Advisory Council
PHE	Public Health England
PHLN	Public Health Laboratory Network
RCPA QAP	The Royal College of Pathologists of Australasia Quality Assurance Programs
WGS	Whole genome sequencing

Preamble

A whole-of-government National Microbial Genomics Framework is required to capitalise on emerging knowledge by better integrating microbial genomics into Australian laboratory and surveillance systems. The National Microbial Genomics Framework 2019–2022 places a strong focus on those policy issues that will benefit from collaboration across all jurisdictions and between public health laboratories and public health units specifically. The framework was developed by the Office of Health Protection within the Department of Health, with input from a joint Public Health Laboratory Network (PHLN) and Communicable Diseases Network Australia (CDNA) Project Reference Group on Microbial Genomics. The group comprises a Commonwealth Chair and nominated members from key jurisdictions.

PURPOSE

This framework is to provide a consistent, national and strategic view for integrating microbial genomics into the Australian health system and for identifying microbial genomics policy issues and challenges that need to be addressed. Developing a whole-of-government and system-focused framework is necessary to ensure consistency across Australia.

The framework will support better coordination and consistency of action between Australian laboratories and public health units to ensure the potential benefits of microbial genomics are harnessed in an efficient, effective, ethical and equitable way.

The framework provides high-level guidance for the development of a nationally agreed microbial genomics system. This system will allow organisms of public health importance to be identified, eventually in real time, within the auspice of a robust quality system. The framework highlights that development of both domestic and international linkages for information sharing and communication are essential to drive this important public health initiative.

The framework is not intended to address all issues related to microbial genomics. Instead, the framework prioritises particular issues for initial consideration and indicates where further work is needed while also recognising that stakeholders have a role in addressing issues independently. Subsequent reviews of the framework are expected to identify other emerging issues.

AUDIENCE

The framework is designed primarily as a tool to provide guidance for the development and implementation of microbial genomic related policies, strategies, actions and services and is directed at decision-makers and policy-makers at national, state and territory and health service levels.

TIME FRAME

The time frame of the framework is three years, with a review anticipated in 2022 to inform the next iteration.

Vision

To protect the health of all Australians from communicable disease and biological agent threats (including foodborne and environmental) through access to microbial genomics information and technology; and, through responsible data sharing, to promote its use for routine surveillance.

Mission

To harness the public health benefits of microbial genomics, genomic knowledge and technology in national public health systems in a consistent, efficient and effective way in order to improve public health responses.

Enablers

To help guide decision-makers and policy-makers in successfully implementing the framework, three key enablers have been identified:

1. **Collaborative governance and leadership**

   Joint national and jurisdictional leadership with engagement from the Australian Government, states and territories, PHLN, CDNA, the Communicable Diseases Genomics Network (CDGN), the Australian Health Protection Principal Committee (AHPPC) and other relevant stakeholders.

2. **Stakeholder engagement**

   Actively engage with private and public health laboratories, research laboratories, clinical diagnostic laboratories, animal laboratories, environmental laboratories, public health units, communicable disease control units, regulatory bodies, OzFoodNet and the Royal College of Pathologists Australasia Quality Assurance Programs (RCPA QAP).

3. **National and international partnerships**

   Establish and maintain genomics collaborations between entities such as PHLN, Australian (counter) Bioterrorism Laboratory Network (ABLN), CDGN and CDNA; related government initiatives such as the Department of Foreign Affairs and Trade's Indo-Pacific Centre for Health Security; and relevant international partners such as the World Health Organization, Public Health England (PHE), the United States Centers for Disease Control and Prevention (CDC) and National Center for Biotechnology Information, the Ministry of Health Singapore, the Public Health Agency of Canada and the Chinese Center for Disease Control and Prevention.

Guiding principles

The development of the framework was supported by the following guiding principles:

i. *National*—developed jointly by Australian and state/territory governments, with the framework facilitating national coordination and government priority setting and decision-making.

ii. *High-level, strategic framework*—identification of themes, principles and considerations for embedding consistency and national coordination as enablers for more efficient, equitable and effective utilisation of microbial genomics. It will be overarching and, as such, will align with existing, or to be developed, regulation, guidelines and discussion papers addressing specific microbial genomics issues.

iii. *System-focused*—an understanding of what the system can deliver and consideration of how a change within one system domain (that is, leadership and governance; system financing; human resources (workforce); information systems; and service delivery) will impact, interact with and change the other domains and affect the system as a whole. This system will be considered within the context of existing capacity and controls to remain consistent with and eventually embed into current communicable diseases surveillance infrastructure.

iv. *Evidence-informed public policy*—ensuring that the best available research and information is used to guide decisions at all stages of policy processes.

v. *Flexible to keep up with scientific advances*—will contain flexibility to enable it to be adapted to reflect the evolving nature of microbial genomics technology and take into account the latest scientific findings and advances and potential shifts in microbial genomics policy issues and challenges.

vi. *Identify priority areas*—gives consideration to prioritising the microbial genomics policy issues and challenges that need to be addressed and identifies directions for change / opportunities for action and areas that require further work.

STRATEGIC CONTEXT

Microbial genomics is already revolutionising the diagnosis, surveillance and control of communicable diseases. The genome of a pathogen reveals at the highest possible resolution its identity and ancestry, the ways in which it infects humans, and how it evades both antibiotic treatment and the immune system.

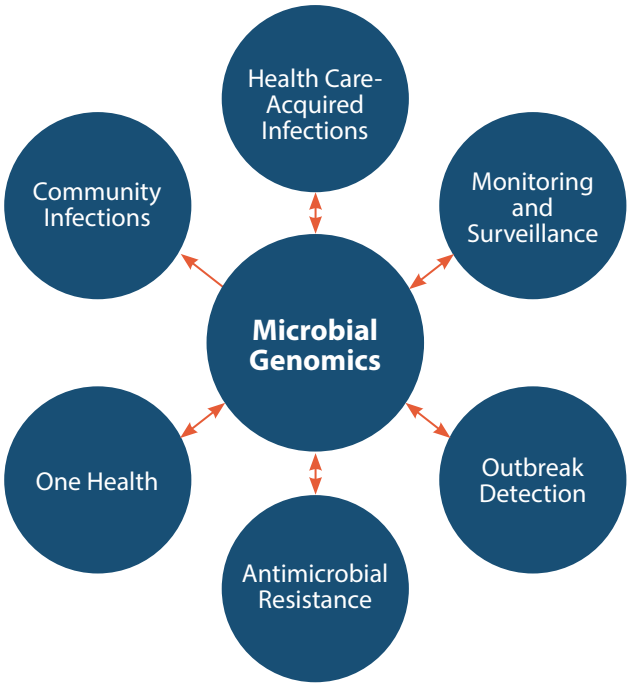

Figure 1. The strategic context of microbial genomics.

The growing accessibility of microbial genomics technology has several potential public health benefits, including:

- the ability to provide high-resolution, nationally and internationally compatible typing and characterisation data for communicable disease surveillance and bio-threat detection
- the ability to eventually use real-time genomic sequencing and genomic surveillance to inform the prevention, early detection and management of disease outbreaks and bio-threats
- the ability to rapidly identify clusters of disease transmission
- more accurate and rapid source attribution and identification of foodborne and waterborne outbreaks
- more rapid detection and characterisation of emerging pathogens or new mechanisms of antibiotic resistance
- the ability to monitor and predict the effectiveness of treatments and vaccines for communicable disease pathogens.

Potential public health applications of pathogen genomics technology may include:

- informing therapeutics and vaccine development
- informing public health infection control in food safety, across hospitals and within community settings
- assisting with the development of agricultural and water resource and management approaches and to determine the persistence of pathogens in the environment
- informing the development of sensitive and specific diagnostic tools
- supporting decision-making in health care service planning
- collaboration with law enforcement agencies in microbial forensics in the context of criminal or terrorist investigations.

The National Microbial Genomics Framework is designed to drive national effort on agreed priorities to provide national coordination of microbial genomic activities across Australia for all priority pathogens regardless of organism type—bacterial, viral or fungal. The framework provides an opportunity to act on divergent approaches to implementing microbial genomics before they form impediments to successful integration of microbial genomics into the Australian health system.

A key enabler for consistency will be the establishment of collaborative governance arrangements that can facilitate actions to address the constantly evolving nature of microbial genomics. The development of support structures will allow for coordination across jurisdictions and between laboratories and public health units.

Currently, the funding for microbial genomics is largely embedded in state-funded health systems. This framework aims to acknowledge the respective responsibilities of all jurisdictions while outlining the need for a collaborative effort to address gaps in activity which will further drive national value.

INTERNATIONAL DEVELOPMENTS

The Public Health Genomics Foundation, a United Kingdom (UK) health policy think tank that is recognised internationally for leadership in the application of genomic technologies to health, has suggested that the implementation of whole genome sequencing (WGS) of pathogens will improve the management of communicable diseases in the following ways:[1]

- Precision—Microbial genomics allows for more specific identification of the bacterium or virus causing an infection and improves the accuracy of outbreak investigation and effectiveness of control measures.
- Sensitivity—Microbial genomics enables the early detection of emerging drug-resistant pathogens and patterns; for example, antibiotic-resistant bacteria or resistant viruses in Human Immunodeficiency Virus patients.
- Speed—For slow-growing bacteria such as *Mycobacterium tuberculosis*, microbial genomics enables significantly faster detection of drug resistance than current culture methods.
- Personalisation—Genomic information can be useful in identifying which drugs will or will not be effective in treating an infection, enabling considerably more effective personalisation of care.
- Detecting novel threats—Genomics is proving to be an important tool in improving detection and understanding of emerging infectious diseases, such as Zika virus, Ebola and avian influenza, in addition to biosecurity threats.

A number of countries have established, to varying degrees, infrastructure and systems to enable nationwide genomic surveillance of communicable diseases and public sharing of genomic data for public health purposes. In particular, the UK (PHE), the United States of America (US) (through the US Food and Drug Administration (FDA) and CDC) and Canada (Public Health Agency of Canada) have been at the forefront of applying microbial genomics to public health microbiology.

CASE STUDY 1: PUBLIC HEALTH ENGLAND

Since the introduction of a centralised WGS service in 2014, PHE has reported significant benefits to and impacts on laboratory services, including improved safety, streamlined laboratory workflows and reduced staffing and equipment costs. The migration to WGS has refined outbreak detection and investigation in laboratories and has improved national and local surveillance of outbreaks and monitoring of the effectiveness of control and preventative measures.[2]

The key approach at both PHE and the FDA has been a hub and spoke model, where coordination and high-level bioinformatics expertise is centralised, with nodes (within different branches of PHE or different laboratories throughout the US) that have capacity for genome sequencing and data analysis that is supported by the central hub. The advantage of this model is the efficient use of scarce bioinformatics expertise, a coordinated approach to data analysis, capacity for rapid data sharing and analysis, and rapid generation of genomics data because isolates can be sequenced at all 'spokes' without the need for transport to other laboratories.

1 Public Health Genomics Foundation (2014), Beating the bugs: the pathogen genomics revolution: http://www.phgfoundation.org/briefing/beating-the-bugs-the-pathogen-genomics-revolution
2 Grant et al. (2018), 'Implementing pathogen genomics: A case study', Public Health England.

CASE STUDY 2: INTERNATIONAL OUTBREAK OF *SALMONELLA* ENTERITIDIS

Near real-time WGS was used to assess the origin of an outbreak of *Salmonella* Enteritidis by determining its strain characteristics. This enabled the identification of linkages between a hospital in England and outbreaks in other countries such as France and Germany. The inclusion of WGS in epidemiological and environmental investigations enabled the tracing of its origin to contaminated eggs from Germany. This informed public health control measures.[3]

There is emerging evidence that demonstrates the benefit of integrating microbial genomics into public health microbiology practice. The cost per genome sequence is rapidly falling and, coupled with improved turnaround times, this revolutionary technology is slowly becoming a viable real-time diagnostic tool.[4]

NATIONAL DEVELOPMENTS

To date, the introduction and implementation of microbial genomics in public health microbiology laboratories in Australia has been sporadic, with varying capacity and capability across jurisdictions. However, over the last couple of years, a number of activities have emerged, all with the aim of facilitating the implementation of microbial genomics technology into routine public health practice.

CASE STUDY 3: MICROBIOLOGICAL DIAGNOSTIC UNIT PUBLIC HEALTH LABORATORY

The Microbiological Diagnostic Unit Public Health Laboratory (MDU PHL) in Victoria is the Australian reference laboratory for Listeria and conducts national definitive testing and WGS-based routine national surveillance for *Listeria monocytogenes*. In 2015, MDU PHL analysed a total of 520 *L. monocytogenes* isolates referred to them from 1995 to 2015. This analysis found that, for national epidemiological surveillance of *L. monocytogenes*, the results inferred *in silico* from WGS data was highly concordant with the results from conventional laboratory typing data. WGS was also able to identify distinct nested clusters within isolate groups that were otherwise indistinguishable. Subsequently, the use of WGS for definitive testing of *L. monocytogenes* was approved as the new national approach for Listeria surveillance, demonstrating that genomics is beginning to replace traditional typing methods for routine public health surveillance and investigation of foodborne pathogens.[5]

3 Inns et al. (2015), 'A multi-country Salmonella Enteritidis phage type 14b outbreak associated with eggs from a German producer: "near real-time" application of whole genome sequencing and food chain investigations, United Kingdom, May to September 2014'. EuroSurveillance, Volume 20, Issue 16.

4 Köser et al. (2012), 'Routine Use of Microbial Whole Genome Sequencing in Diagnostic and Public Health Microbiology'. PLoS Pathogens, Volume 8, Issue 8, p. 1.

5 Kwong et al. (2016), 'Prospective Whole-Genome Sequencing Enhances National Surveillance of Listeria monocytogenes'. Journal of Clinical Microbiology, Volume 54, Issue 2, pp 333–342.

CASE STUDY 4: MULTIJURISDICTIONAL OUTBREAK OF *SALMONELLA* HVITTINGFOSS IN ROCKMELONS

In 2016, an increase in *Salmonella* Hvittingfoss infections was identified through routine surveillance in New South Wales and across two other jurisdictions. Based on epidemiology and traceback investigation, rockmelons were found to be the probable cause. Over 150 cases of salmonella were associated with the outbreak and WGS was used to definitively link 110 human cases of *S.* Hvittingfoss infection to each other and to the affected rockmelons. This marked the first time WGS was used in Australia to investigate multi-jurisdictional outbreaks of foodborne disease.[6]

Since July 2015, CDGN, a network of public health laboratories and other stakeholders in Australia, has been meeting through a series of teleconferences, annual face-to-face meetings and symposia with the specific aims of:

- establishing a unified and coordinated public health microbial genomics network to advise and interact with existing laboratory and public health networks, government, policy-makers and other relevant stakeholders
- establishing consensus on WGS and metagenomic platforms and methods
- coordinating jurisdictional capacity and expertise in microbial WGS and metagenomics
- establishing consistent, validated national microbial bioinformatics pipelines
- developing procedures and policies allowing rapid national genomic data sharing and analysis in an ethical framework
- developing and supporting teaching and training activities to enhance public health microbial genomics.

CDGN has representative membership from all jurisdictions, with observer members from the Australian Government and the New Zealand national public health laboratory (ESR). CDGN has been formalised as an expert reference panel reporting to PHLN and is currently coordinated by MDU PHL. To address the aims of the network, CDGN has established a number of working groups covering the following topics:

- workforce training and curriculum development in microbial genomics
- development of a secure platform for rapid, equitable and ethical data sharing ('AusTrakka')
- standardisation and implementation of genomic technologies in laboratories (including clinical metagenomics). This includes development and support for the RCPA QAP in microbial genomics.

6 Australian Government Department of Health, Annual Report 2016–2017.

CASE STUDY 5: LISTERIA IN ROCKMELONS—OUTBREAK INVESTIGATION

In 2018, WGS was used to investigate the origin of 22 human cases of listeriosis in Australia. Laboratory testing was referred to MDU PHL, which found through WGS that the *Listeria monocytogenes* strain causing the infections was related to isolates recovered from 37 rockmelons sourced from retail and wholesale outlets that were supplied by the same farm. The use of WGS enabled the identification of the outbreak origin and informed post-outbreak controls to prevent further risk of illness.[7]

CHALLENGES IN THE AUSTRALIAN CONTEXT

- There is a lack of national coordination of microbial genomic activities across Australia.
- There is a need to determine a list of priority pathogens of public health importance.
- Public health laboratory and health unit systems do not currently have the capacity or capability to fully integrate microbial genomics data and metadata into existing surveillance systems.
- Implementation of microbial genomics has been organisationally disruptive through replacement of traditional testing methodologies and placing complex molecular analysis at the forefront of communicable disease prevention and control.
- There is an essential need to undertake workforce planning and training in bioinformatics for laboratory scientific staff and epidemiologists.
- There is a need to develop policies and procedures quickly to enable rapid national genomics data sharing and analysis to enhance public health surveillance and response.
- There is a role for national standardisation and definition of quality practices to assist in National Association of Testing Authorities (NATA) accreditation of microbial genomics analysis in public health laboratories in Australia.
- There is a need for exploration of opportunities to integrate microbial genomic data into surveillance infrastructures (for example, OzFoodNet, the National Notifiable Diseases Surveillance System, jurisdictional health databases, the National Tuberculosis Advisory Committee and the National *Neisseria* Network).
- There are differences in jurisdictional capacity, methodology, instrumentation, governance structures and requirements for microbial genomic technologies and information within both the laboratories and public health units.

7 NSW Department of Primary Industries, Biosecurity & Food Safety (2018), 'Listeria Outbreak Investigation—Summary Report for the Melon Industry, October 18', NSW Department of Primary Industries.

Strategic priorities

The National Microbial Genomics Framework outlines five strategic priorities that give consideration to prioritising the microbial genomics policy issues and challenges that need to be addressed. They also identify directions for change and opportunities for action as well as areas that require further work. The priority areas are not necessarily discrete and there will be interrelationships and interdependencies.

The five strategic priorities are as follows:

- *Strategic Priority 1*—Standardised National Approach
  - Establishing governance arrangements to drive standardisation on microbial genomics matters of national significance, including rapid national data sharing.
  - Growing and applying microbial genomic knowledge that is evidence based, standardised and of high quality.
- *Strategic Priority 2*—Technology and Data Governance
  - Establishing nationally agreed and standardised data governance arrangements.
  - Promoting the importance of ethical and equitable data sharing and understanding the risks (or perceived risks) that it may entail.
  - Building high-performance computing infrastructure to support data storage and sharing that can adapt to enhancing microbial genomics technologies.
- *Strategic Priority 3*—Integration into Public Health
  - Ensuring collaboration and strong linkages between Australian laboratories and public health units to ensure the value of microbial genomics technology is recognised. Integration and planning with non-human testing laboratories is also desirable.
  - Establishing nationally consistent reporting structures that are compatible with existing public health surveillance systems.
- *Strategic Priority 4*—Access and Workforce
  - Building and maintaining a competent multidisciplinary microbial genomics workforce.
  - Ensuring microbial genomics capacity and capability is equitable across jurisdictions.
- *Strategic Priority 5*—Financing
  - Ensuring the funding model applied to microbial genomics considers the substantial establishment costs and is cost-effective and sustainable into the future.

The following values underpin the strategic priorities of the framework:

- The application of microbial genomic knowledge is ethically, legally and socially responsible.
- Access to microbial genomics information is equitable within and between the states and territories and the Australian Government.
- The application of microbial genomics knowledge to improve public health outcomes is supported and informed by evidence and research.

Strategic Priority 1— Standardised National Approach

Fragmentation in current public health surveillance activities is exemplified by jurisdictional differences in specimen flow, public health microbiology service reimbursement and epidemiological typing and characterisation. These result in considerable national variability in testing practices, turnaround times and reporting.

The recent introduction of microbial genomics into public health laboratories offers a window of opportunity to ensure national coordination and consistency in the application of microbial genomics to public health. Some of the key risks of allowing microbial genomics to develop across jurisdictions without national coordination and standardisation include:

- inconsistency in analysis due to different bioinformatics pipelines
- incompatible data from different sequencing platforms
- inconsistency in the application of microbial genomics to public health and bio-threat issues
- fragmentation in data collection and storage
- lack of consistency in data analysis and output for surveillance and investigative efforts
- lack of collation and curation of national-level genomic data.

Some of the key challenges in achieving nationally consistent laboratory-based surveillance have been highlighted in the National Framework for Communicable Disease Control. These include:

- aligning governance and reporting models for public health laboratories and national centres
- harmonising laboratory-based surveillance methods between jurisdictional public health reference laboratories
- agreeing on an ethical and confidentiality dimension
- improving information sharing between laboratories, public health authorities and clinicians
- agreeing on sustainable financing mechanisms for public health laboratory activities.

OUTCOME 1.1—ESTABLISHMENT OF STANDARDISED POLICIES AND PROCEDURES

- Develop common standards, nomenclature and reporting outputs and formats that are fit for purpose for public health surveillance and response.
- Agree on a national open-source platform which hosts bioinformatics pipelines and a data repository that is available to all public health laboratories.

OUTCOME 1.2—HARMONISATION OF LABORATORY-BASED SEQUENCING AND SURVEILLANCE METHODS

- Develop harmonised laboratory-based sequencing methodologies.
- Develop standardised microbial genomics surveillance methods.

OUTCOME 1.3—ESTABLISHMENT OF QUALITY SERVICES

- Develop quality assurance and proficiency testing specific to microbial genomics.
- Enhance technical competence and integrity within organisations offering microbial genomics services through collaboration with National Pathology Accreditation Advisory Council, NATA and RCPA QAP.
- Promote sharing of sequence data nationally and with international laboratories to inform detection and investigation of multi-country outbreaks.

What does the future look like?

- The application of microbial genomics to public health—communicable disease and biological agents of security concern control—is well understood by stakeholders.
- A coordinated and consistent approach has been developed around the application of microbial genomics in public health practice that increases efficiency and reduces duplication of effort.
- The approach has been adopted at a national level.
- The approach is sustainable and well supported by information technology (IT) infrastructure, quality assurance pathways and appropriate financing.

Strategic Priority 2—Technology and Data Governance

There is recognition in the public health community of the importance of data sharing to improve public health surveillance and response. Identifying suitable approaches to data sharing that ensure sensitive data remains protected while allowing for the benefits of genomic data to accrue in public health is an ongoing challenge. Currently, data sharing happens in an ad hoc manner within negotiated bilateral state and territory agreements or other undocumented arrangements. The microbial genomics data exchanged in this manner has been used as a tool for outbreak investigation and, more recently, outbreak detection. While it has allowed for finer resolution of outbreaks, and greater confidence in including or excluding isolates in a particular outbreak, microbial genomics data has not been used extensively as a tool for detecting outbreaks. The ultimate aim is to achieve real-time sequencing and data exchange to enable enhanced outbreak detection and response. The value of genomic data, collected as part of genomic surveillance, for basic research and activities aligned with the One Health approach should be also acknowledged.

A survey was conducted in 2017 to inform the PHLN report *Data sharing to improve decision making in public health: A case for Australian Public Health Laboratories*. The report discusses support for a model of real-time data sharing to a central repository with controlled access across the laboratory network and relevant government agencies, which would allow approved users to curate and analyse data relevant to local and national surveillance of foodborne pathogens and antimicrobial resistances.[8]

OUTCOME 2.1—TECHNOLOGY

- Acquire and maintain comparable sequencing instruments across jurisdictions which have the flexibility to be configured for use in the Australian setting.
- Develop and maintain high-performance computing infrastructure to support data storage and sharing that can adapt to emerging microbial genomics technologies.

OUTCOME 2.2—DATA SHARING

- Enable multi-directional microbial genomic data and critical metadata sharing across and within jurisdictions, to the Australian Government and internationally, including the provision of data and/or isolates to public health laboratories from non-reference laboratories.
- Develop an agreed national protocol for sharing isolates and/or genomic, phenotypic, and epidemiological metadata.
- Ensure data sharing is compliant with the appropriate national and jurisdictional legislation and guidelines such as the *Privacy Act 1988*, the *National Health Security Act 2007*, the *National Statement on Ethical Conduct in Human Research* (2007) and any organisational ethical frameworks for public health practice.

8 Public Health Laboratory Network (2017). 'Data sharing to improve decision making in public health: a case for Australian Public Health Laboratories', not publicly accessible.

OUTCOME 2.3—DATA STORAGE

- Develop nationally agreed standards for data collection, safe storage, data sharing, custodianship, analysis, reporting and privacy requirements.
- Develop infrastructure to support secure storage of microbial genomic data.

OUTCOME 2.4—USE OF DATA

- Agree upon common standards for the public health use of microbial genomics data across jurisdictions.
- Agree upon common reporting standards for microbial genomics.
- Agree upon a common reporting format across laboratories and jurisdictions.

OUTCOME 2.5—DATA GOVERNANCE

- Review legislation and regulation at both state and federal levels to identify whether there are any impediments to implementation of microbial genomics, particularly in relation to data sharing.
- Ensure microbial genomics outcomes are achieved to the greatest extent possible.
- Support discussions for implementation of a national governance structure.
- Ensure data are being handled in an ethical and culturally appropriate way.
- Ensure meaningful and appropriate recognition of data sources by both primary and secondary users.
- Establish trust between data-sharing entities and encourage further data sharing among active and potential providers.
- Ensure data privacy and security is maintained throughout the data collection, handling and storage process.

What does the future look like?

- A national data governance mechanism is in place to ensure appropriate data sharing and data use in the nationally consistent application of microbial genomics in public health practice.
- Systems and IT infrastructure is established to support current and future data sharing and storage requirements nationally and internationally.

Strategic Priority 3— Integration into Public Health

The main utility of microbial genomics is in enhancing national and international surveillance and response to communicable diseases. The use of sequencing data has the capacity to form the basis of robust public health surveillance through rapid pathogen detection and identification; and monitoring that ultimately links to information on clinical, demographic and exposure details.

To achieve maximal public health impact, it is critical that genomic data are appropriately linked to epidemiological and clinical data and that results from genomic data are rapidly disseminated back to 'end users' or even directly accessible.

Conceptually, this is directly aligned with several of the key outcomes in the National Framework for Communicable Disease Control, however will require strategic coordination and collaboration between existing groups and networks.

Given the vast amount of useful data that microbial genomics generates (related to pathogen transmission, resistance, virulence and evolution) and the increasing popularity of culture-independent diagnostic tests in clinical laboratories and its potential impact on laboratory-based typing, microbial genomics sits directly at the interface between clinical epidemiological surveillance and laboratory-based surveillance. As such, it is critical that microbial genomics is integrated into existing epidemiological networks, as this would better enable:

- proactive and coordinated gathering and sharing of information
- detection and rapid response to disease outbreaks
- identification of disease clusters
- accurate and rapid source identification of foodborne and waterborne outbreaks
- accurate and rapid source attribution of foodborne and waterborne outbreaks
- rapid detection and characterisation of emerging pathogens or new mechanisms of antibiotic resistance.

OUTCOME 3.1—INTEGRATION OF MICROBIAL GENOMICS DATA INTO EPIDEMIOLOGICAL SYSTEMS

- Facilitate integration into epidemiological and antimicrobial resistance surveillance systems.
- Facilitate integration into laboratory information systems.
- Facilitate integration into food safety and regulatory sector arrangements.
- Facilitate integration into animal health sector arrangements.

OUTCOME 3.2—IDENTIFICATION OF PRIORITY ORGANISMS

- Determine a list of priority organisms through consultation and collaboration with PHLN, ABLN, CDNA, CDGN, AHPPC, the Australian Strategic and Technical Advisory Group on AMR, OzFoodNet, the Australian intelligence community, research organisations and other relevant stakeholders to identify where sequencing provides an enhanced public health benefit over existing laboratory methodologies.
- Facilitate the rapid detection and characterisation of emerging and/or newly imported pathogens and other bio-threats.
- Improve knowledge on what type of microbial genomics information improves public health disease control and response and how this is applied in relation to priority organisms, particularly its role in maintaining national health security and biosecurity.
- Facilitate and encourage private microbiology laboratories to share microbial genomics related data for public health and surveillance purposes for priority organisms.

OUTCOME 3.3—PRIORITISATION OF PUBLIC HEALTH MICROBIAL GENOMICS RESEARCH

- Enhance communication with microbial genomics researchers to identify gaps for improvement in disease control for public health purposes.
- Maximise microbial genomics research opportunities to enhance public health outcomes.
- Ensure early identification of translational research priorities in microbial genomics.

What does the future look like?

- Microbial genomics is fully integrated into national public health practice.
- There is evidence from Australia that microbial genomics has contributed to improvements in the detection of outbreaks and enabled timely response.
- There is greater systematic collaboration with researchers and a process to maximise opportunities for improvement and expansion in the application of microbial genomics.

Strategic Priority 4—Access and Workforce

Currently, public health microbiology services are provided by public health laboratories through a network of jurisdictional specialist microbiology laboratories. These public health laboratories are either dedicated specialist (reference) facilities or are co-located within hospital-based facilities. Depending on jurisdictional size and capacity, public health laboratories provide a range of specialist functions, including:

- detailed typing and characterisation of communicable disease pathogens, underpinning national surveillance for communicable diseases
- laboratory contribution to outbreak investigation
- specialised reference diagnostics and confirmatory testing
- provision of scientific advice to public health networks and authorities
- state-based and national leadership in standardising the diagnosis and laboratory-based surveillance of communicable disease
- identification and application of new technological and scientific developments to public health microbiology practice.

There is varying capacity and capability across jurisdictions with regard to the introduction and implementation of microbial genomics in public health laboratories. The implementation of microbial genomics services requires access to high-performance computing infrastructure, and many diagnostic and reference laboratories may not have this access. At present, three jurisdictions have been identified as performing microbial genomics as part of routine public health microbiology activities for specific pathogens and are the most developed in terms of capability, capacity and experience (Victoria, New South Wales and Queensland). This is probably due in part to initial demand.

The emergence of portable sequencing platforms and decentralised molecular diagnostic testing will challenge the traditional model of clinical sample referral to public health laboratories for specialist typing and characterisation as part of surveillance activities. Common protocols and collaboration between the clinical and public health laboratories will be key to ensuring quality and portability of genomic data across integrated laboratory information systems for surveillance purposes.

A growing number of pathology providers in public and private sectors are considering different models of genomics testing for hospital infection control and antimicrobial stewardship.

OUTCOME 4.1—ENHANCED CAPACITY AND CAPABILITY

- Assess, foster, establish and maintain national microbial genomics capacity and capability.
- Ensure equitable access to capability, including high-performance computing infrastructure, for all jurisdictions.
- Develop bioinformatics expertise, noting that this cannot be generalised across organism types.
- Maintain and build upon engagement with private laboratories.

OUTCOME 4.2—STANDARDISED MICROBIAL GENOMICS EQUIPMENT AND EXPERTISE

- Maintain comparable instrumentation across jurisdictions.
- Maintain comparable levels of expertise across jurisdictions.

OUTCOME 4.3—ENCOURAGE INNOVATION

- Promote national and international collaboration and innovation across laboratories, public health units and academia to keep pace with advances in microbial genomics technology, including non-culture-based approaches, in future.

OUTCOME 4.4—WORKFORCE DEVELOPMENT

- Promote establishment, improvement and maintenance of genomics literacy and related skills in both laboratory and non-laboratory settings (for example, public health clinicians and epidemiologists) through microbial genomics education, training and quality assurance.
- Promote workforce training strategies and planning to ensure consistent and equal access to upskilling opportunities across jurisdictions and microbiology service providers.
- Facilitate collaboration, partnerships and networks between professional colleges and societies to promote and support the sharing of knowledge.

What does the future look like?

- A robust, sustainable national microbial genomics capacity and capability has been established to meet public health need.
- Capacity and capability is well supported and will be maintained through national standardisation of equipment and levels of required expertise and workforce development.
- Microbial genomics literacy is maintained across all relevant stakeholders and there is national support for innovation.
- The genomics workforce is supported throughout all stages of their careers, building a well-trained and microbial genomics literate workforce to meet the increasing demand for genomics services in Australia.

Strategic Priority 5—Financing

Public health laboratories have identified common challenges to the routine implementation of microbial genomics in their laboratories. These include:

- lack of sustainable funding for initiating and maintaining a microbial genomics service in public health laboratories, particularly in those that receive relatively low specimen numbers
- limited bioinformatics expertise in some jurisdictions
- limited infrastructure in some jurisdictions in relation to sequencing, data storage and computational capacity
- lack of standardisation of bioinformatics analysis between jurisdictions
- lack of coordination of genomics activities at a national level.

Sustainable funding is essential for the success of a nationally consistent and comprehensive microbial genomics program. In May 2018, the Australian Government announced an investment of $500 million over 10 years for an Australian Genomics Mission under the Medical Research Future Fund. The Australian Genomics Mission will help to save or transform the lives of more than 200,000 Australians through research on better testing, diagnosis and treatment. The initial focus of the Australian Genomics Mission is on human health genomics; however, submissions related to microbial genomics will be invited and considered from a translational research perspective.

While the added value of microbial genomic services for public health has been recognised, the value reimbursement models remain underdeveloped. The central funding arrangements employed by the US CDC and PHE may not be fully applicable in Australia. Agreement needs to be reached between clinical and public health services with regard to funding for service development and delivery where the microbial genomics services have a dual clinical and public health benefit—for example, drug resistance and antimicrobial stewardship.

OUTCOME 5.1—ESTABLISHMENT OF A SUSTAINABLE FUNDING MODEL

- Develop a sustainable funding model involving a partnership between the Australian Government and the states and territories.
- Improve flexibility to keep pace with advances in technology and the expanding role of microbial genomics.

OUTCOME 5.2—ESTABLISHMENT OF COST-EFFECTIVENESS

- Ensure the cost of introducing and maintaining microbial genomic technology results in savings accrued from improvement in patient care and replacement of existing technologies. Initial implementation will result in a short-term increase in costs while development of new workflow processes and replacement of outdated testing methods occur.

What does the future look like?

- A sustainable funding model has been established, linked to broader public health laboratory testing, outbreak investigation and public health response.
- The funding model is agile so it can respond to emerging technologies and expanding application of microbial genomics to public health.

Implementing the framework

The National Microbial Genomics Framework sets out how the Australian Government and the states and territories will work collaboratively to integrate microbial genomic approaches into health care over time. While the policy framework outlines an agreed national approach to policy, regulation and funding for microbial genomics, it does not identify all of the specific actions needed to take the framework forward.

Following endorsement of the framework, an implementation plan will be developed to identify actions, responsibilities, time frames, priorities and resourcing. An implementation plan will be a key tool to measure the progress and success of the framework and allow for the monitoring of national and jurisdictional progress against activities and milestones outlined.

It is intended that every three years the Australian Government and the states and territories will evaluate the activity outcomes described in the framework and implementation plan, including the cost-effectiveness, key achievements, sustainability and challenges of integrating microbial genomics into the Australian public health system.

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All information in this publication is correct at June 2019

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