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Biography

Prior to retirement, **John Bates** specialised in the examination of micro-organisms of public health significance in clinical, food, water and environmental samples, including *Giardia*, *Cryptosporidium* and *Legionella*. Other areas of expertise included laboratory-based outbreak investigations, notifiable pathogens and

bioterrorist agents referred to the laboratory for identification and typing. He ran a complex surveillance system for *Salmonella* infections across the State, and the tools of outbreak investigation and surveillance can be readily applied to intentional releases. Through his involvement with the Public Health Laboratory Network of Australia (which he has chaired twice), the Australian (counter) Bioterrorism Laboratory Network and the US Laboratory Response Network, he played a key role in the development of a capability within Queensland to identify bioterrorist bacterial agents and toxins in a timely manner. As a result, he provided expert advice to Queensland Health and to laboratory clients, as well as reports, based on the monitoring of trends of known diseases and the emergence of new diseases, to health authorities and clients.

A decade of RCPAQAP Biosecurity improving testing for biological threats in Australia



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Abstract. Biosecurity is a term broadly applied to the protection, control and accountability of biological agents and toxins to minimise the risk of their introduction through natural, unintentional (accidents) or deliberate processes. Biosecurity protection involves the engagement of all stakeholders including government, public health networks, industry, and scientific community. While the Commonwealth Government primarily manages biosecurity, it is also a shared responsibility with State and Territory governments. Rapid, accurate diagnosis is essential to informing all levels of response to biosecurity threats. External quality assurance (EQA) through proficiency testing (PT) is an indispensable tool to allow assessment of laboratory performance. This ensures laboratory capability and capacity are in a constant state of readiness to effectively detect biological threats and reduce the impact and transmission of disease. Since 2009, the Royal College of Pathologists Australasia Quality Assurance Program (RCPAQAP) has been contracted by the Australian Government Department of Health to establish a proficiency testing program (PTP) for the detection of biological threat agents. Starting out as a PTP for the detection of *Bacillus anthracis*, RCPAQAP Biosecurity has undergone significant transformation, thereby building and enhancing laboratory preparedness. Alterations in the program have been in line with the changing landscape of biosecurity and other emerging infectious diseases across Australia, and worldwide.

Launched in June 2009, RCPAQAP Biosecurity is funded by the Australian Government's Department of Health. It was initially founded to establish a proficiency testing program (PTP) exclusively for the detection of *Bacillus anthracis*. In 2012, RCPAQAP Biosecurity's scope was extended to offer PTP for biological agents of security concern, other potential agents, and emerging

communicable disease threats. These PTP have been shown to be valuable tools for a laboratory's continuous improvement process, through its role in supporting public health measures implemented by the Australian government. As such, the program is an integral component of state and national efforts to prepare, respond to and mitigate potential threats concerning natural or human-enabled outbreaks of disease. It plays an important part of ensuring that the front line of defence (hospitals and laboratories) have the necessary skills, knowledge and technologies to accurately detect the presence of a biothreat and protect the Australian community, through the incorporation of PTP and close collaboration with the Department of Health, the Public Health Laboratory Network (PHLN) and the Australian (counter) Bioterrorism Laboratory Network (ABLN).

Over the past decade, RCPAQAP Biosecurity has responded to the changing landscape of biothreats, by offering an extended range of specialised PTP. Figure 1 provides a snapshot of the timeline (Figure 1a) and summary (Figure 1b) of programs introduced by RCPAQAP Biosecurity. Since 2009, RCPAQAP Biosecurity has offered a total of 95 programs including 78 specimen modules, 11 virtual modules and 6 eLearning modules, which collectively have covered over 25 different Security Sensitive Biological Agents (SSBAs) and other pathogenic organisms (Figure 2). The growing number of programs offered is directly linked to risk associated with the emergence of new disease threats of clinical relevance (e.g. Middle East respiratory syndrome, Zika virus disease), and the re-emergence of diseases causing significant outbreaks (e.g. Ebola outbreak in West Africa, *Yersinia pestis* outbreak in Madagascar).

Rapid advancements in biotechnology, such as the introduction of whole genome sequencing (WGS), were also a major

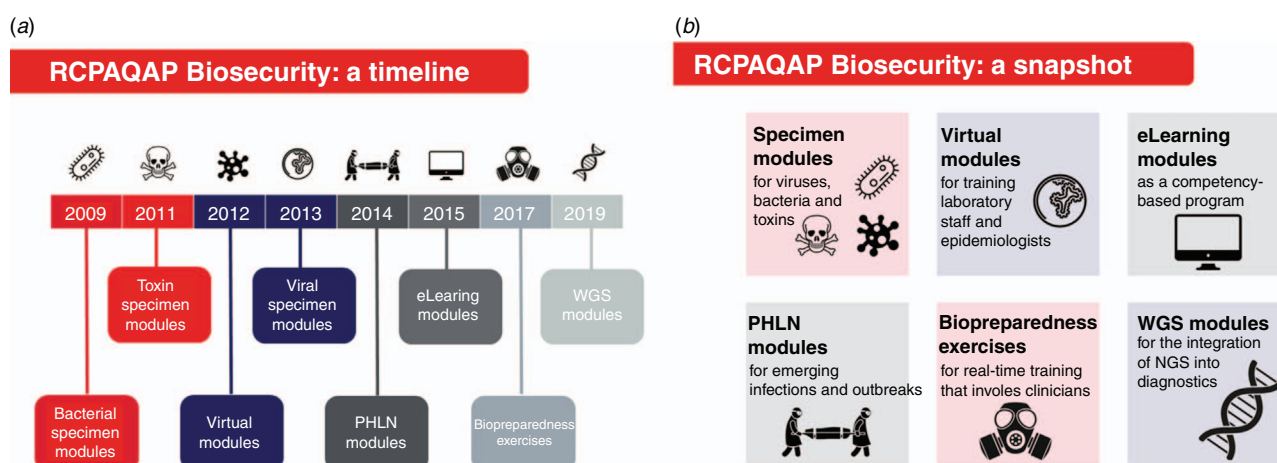


Figure 1. Timeline (a) and summary (b) of programs introduced by Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) Biosecurity.

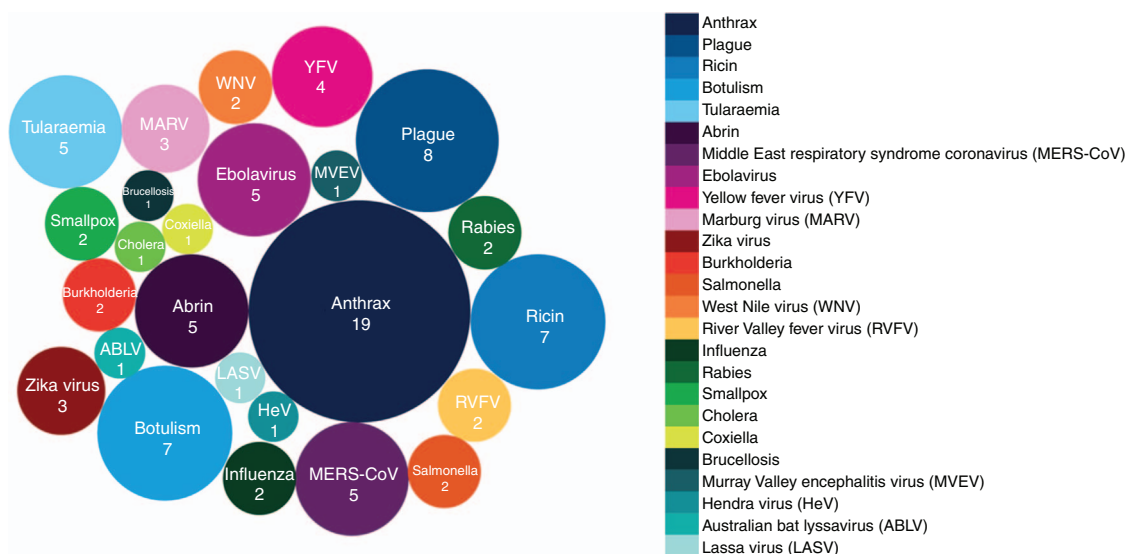


Figure 2. The number of QA modules (specimen, virtual and eLearning) offered for biosecurity relevant diseases, organisms and toxins. ABLV, Australian bat lyssavirus; HeV, Hendra virus; LASV, Lassa virus; MARV, Marburg virus; MERS-CoV, Middle East respiratory syndrome coronavirus; MVEV, Murray Valley encephalitis virus; RVFV, Rift Valley fever virus; WNV, West Nile virus; YFV, yellow fever virus.

consideration in the development of PTP programs offered by RCPAQAP Biosecurity. In 2018, RCPAQAP Biosecurity, in collaboration with the Communicable Diseases Genomic Network (CDGN), developed a pilot PTP for detection and analysis of a bacterial isolate (*Salmonella enterica*) using WGS. The program was established to assist laboratories with the introduction of a genomics workflow which requires a set of measurable and assessable references of quality standards. It provided valuable insight into the current application of WGS in Australian laboratories and a means for the evaluation of laboratory results that meet minimum quality standards within the areas of sequencing and bioinformatic processes. The pilot PTP was crucial to assist in developing standardised measures for the integrated WGS workflows, including pre-analytical (DNA isolation and library preparation), analytical (quality metrics of the sequencing run) and post-analytical (data analysis) processes, where different measures and standards are applicable¹. Different software packages used by laboratories in the post-analytical phase can cause heterogeneous results. Therefore, EQA such as the WGS pilot PTP are important in addressing the development of standardised quality control and data interpretation, which remains the biggest challenge in fully realising the potential of WGS analyses for clinical and public health microbiology laboratories of all scales².

The recent emergence of the novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has highlighted the importance of public health preparedness for emerging infectious diseases threats in Australia. Laboratory preparation for large-scale testing of SARS-CoV-2 through the provision of QAPs during the coronavirus

disease (COVID-19) pandemic is in line with the RCPAQAP Biosecurity commitment to the Australian Government's Department of Health to support public health measures and prepare for local community transmission. There have been two rounds of PTP for SARS-CoV-2; round 1 was offered to selected PHLN laboratories across Australia and New Zealand on 2 March 2020, while round 2 was offered on 12 May 2020 to both public and private Australian laboratories free-of-charge. Round 1 of this program was offered 32 days after the COVID-19 outbreak was declared a public health emergency of international concern (PHEIC) by the World Health Organization (WHO).

Being a dedicated PTP for biosecurity specialised modules, RCPAQAP Biosecurity has demonstrated the importance of EQA by developing and offering PTPs that identify the limitations in the detection methods used for testing SSBA and other pathogens. It also highlights the need for new diagnostic tests and assists in the future use of new technologies. Detection using the necessary diagnostic equipment or kits and reagents to accurately detect these agents, in particular toxins listed as Tier 1 SSBA (Botulinum toxin, Ricin and Abrin) which are considered to pose the highest security risk to the Australian public health, has proven to be challenging in the past. EQA activities performed at RCPAQAP Biosecurity, such as the development of new PTP were important to support the need for laboratories to conclusively identify these toxins. With integrated sample preparation, amplification, detection and analysis, alternative detection methods for these toxins were proposed and applied across public health laboratories for diagnostic use.

The PTP offered by RCPAQAP Biosecurity were often developed in response to a disease outbreak, thereby facilitating quality assurance of newly developed laboratory methods and ensuring laboratories can deliver accurate diagnosis. This urgency puts significant strain on EQA providers, which are limited by the lack of availability of live organisms or inactivated low-risk clinical isolates to include in a PTP panel, as well as the restrictions associated with biocontainment and importation³. To address these limitations, RCPAQAP Biosecurity investigated and pioneered the use of simulated specimens containing RNA transcripts in EQA. These specimens were used in the 2013 MERS-CoV Specimen Module, and in a PTP for the detection of *Ebolavirus* (EBOV), which was offered in April 2014, four months before the WHO declared the Ebola outbreak in West Africa a PHEIC. Using these synthetic specimens was a key factor that enabled RCPAQAP Biosecurity to develop new PTP in response to viral disease outbreaks in a timely manner, without the need to acquire the etiological agent of the disease.

Advances in life sciences such as synthetic biology and genome editing applicable in health and medicine are shaping the biosecurity field, which already have a few precedents of analytical tools⁴. A fundamental aspect of biosecurity is understanding and managing these potential risks to Australia's national health, where regulation and mitigation are a challenge. The role of RCPAQAP Biosecurity is to recognise the expanding suite of biological threats and provide smart and efficient PTP that are ahead of, or in line with, the rapidly evolving changes in laboratory testing in molecular microbiology and biosecurity fields. Moving forward in the 'Digital Age', it is crucial for RCPAQAP Biosecurity to develop appropriate competency-based programs (i.e. development of knowledge and skills) that utilise the rapid advancements in computing technology. Studies have shown that audio-visual methods of teaching create a disciplined learning environment which fosters effective engagement of participants⁵. First developed in 2015, RCPAQAP Biosecurity now offers eLearning modules for nine of the thirteen SSBAs. Catering to the modern learner preferences, these online modules are made available throughout the year to allow the education of public and private laboratory personnel and the Royal College of Pathologists (RCPA) microbiology registrars.

RCPAQAP Biosecurity has been the leading provider of EQA for biological agents of security concern for the last decade, and has been an integral component of Australian biosecurity activities. Through its virtual and eLearning modules, it has increased its global reach and accessibility, thus contributing to global capacity building. Continual participation in PTP offered by RCPAQAP

Biosecurity ensures Australian laboratories are aware of what to do and who to inform if a biosecurity or bioterrorist threat with an SSBa is suspected. RCPAQAP Biosecurity regularly reviews these PTPs, looking for new and innovative opportunities in order to add value to what is offered to participants and to protect national security. The excellent results reported by participating Australian laboratories reinforces the view that Australia has an excellent public health laboratory system. However, it is paramount that laboratories remain vigilant and are equipped with the most up-to-date knowledge and resources for the accurate detection of biological agents.

Conflicts of interest

The authors declare no conflicts of interest.

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Biographies

Dr Katherine Lau was awarded her PhD in Medicine for her research on the biology and molecular biology of new recombinant viruses of HIV from the University of Sydney in 2009. She then completed her postdoctoral research training at the Kolling Institute of Medical Research, University of Sydney in 2013. Dr Lau's main expertise is primarily on the application of advanced molecular biology technique in virus research. Her passion has always been to incorporate the principle and technical knowledge into her roles for a better disease and diagnosis outcome. Dr Lau has been with the RCPAQAP Biosecurity since 2013. At present, she is responsible for the Viral Specimen Program, including ongoing research, development, and evaluation of new and existing Proficiency testing programs. In 2018, Dr Lau led and developed a pilot PTP for detection and analysis of

a bacterial isolate using Whole Genome Sequencing, in collaboration with the Communicable Diseases Genomic Network.

Dr Torsten Theis is a Senior Scientist at the Biosecurity Department of the RCPAQAP. He received his PhD in Molecular Microbiology from the Berlin University of Technology (Germany). A post-doctorate fellow at University Colleges London (UK), University of Sydney and University of Technology Sydney, he investigated different aspects of the multidrug resistant phenotype of *Staphylococcus aureus*. Dr Theis joined RCPAQAP in 2010, and is currently responsible for all program aspects that require PC3/PC4 laboratory work, including researching, evaluation, and preparation of specimens to be used in the Proficiency testing programs (PTP) offered by the Biosecurity Department of the RCPAQAP. He liaises with leading specialists in the fields of public health, forensics and counter-bioterrorism, researching current issues and authoring educational material and reports. In collaboration with the Laboratory Strengthening and Biorisk Management department at the World Health Organization, Dr Theis is the RCPAQAP project lead for the development of PTPs for the detection of arboviruses, coronaviruses, and agents responsible for viral haemorrhagic fevers.

Dr Alexa Kaufer graduated with a Bachelor (Honours) of Forensic Biology in Biomedical Science in 2015. She received her PhD in parasitology from the University of Technology Sydney in 2020, investigating the use of kinetoplast DNA molecular systematics, species identification and diagnostics of trypanosomatid parasites. She began her role as a scientist at the Biosecurity Department of the RCPAQAP in 2019.

Joanna Gray has a Bachelor of Applied Science majoring in Microbiology from the University of Technology, Sydney. She has approximately 40 years' experience in microbiology and quality

management, a black belt in six sigma and lean, a broad range of experience in training and other business improvement roles in the pharmaceutical and medical industries. For the past 20 years Joanna has been an accredited Evaluator for Business Excellence Australia who annually host the Australian Business Excellence Awards. Since 2009 Joanna is the RCPAQAP Biosecurity Program Manager providing Australia, and a select number of overseas laboratories, with proficiency testing surveys and educational modules for SSABs, other potential agents and emerging communicable diseases threats to Australia. The Biosecurity program is funded by the Australian Government's Department of Health. Since 2018 Joanna assumed the additional role of RCPAQAP Manager- Molecular Infectious Diseases. Since 2019 Joanna has taken on the added responsibility for the Molecular Genetics programs as RCPAQAP Manager- Molecular Genetics.

Professor William Rawlinson, AM FAHMS BSc(Med) MBBS PhD (Cantab) GCM FRACP FRCPA FASM FFSc, is Director of Serology and Virology Division (SAViD), Director Organ and Tissue Donor screening laboratory, Director NSW State Reference Laboratory for HIV, Chair Biosecurity Quality Assurance Program RCPAQAP, Deputy Chair Serology Quality Assurance Program RCPAQAP, Chair National Verification Committee for Measles and Rubella. William Rawlinson is a clinician scientist researching viral pathogenesis, particularly respiratory viral infections, congenital infections, and enteroviruses in type 1 diabetes mellitus. He established, and oversees, serology and virology clinical research programs, statewide transplant donor screening, and national quality programs for serology and biosecurity. He is conjoint professor at UNSW with over 400 publications and over 18 000 citations from his publications in basic research, diagnostic and clinical virology.

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