2021 - 2022

Annual Report

World leader in the Science of Quality

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SVI St Vincent's Institute MEDICAL RESEARCH

NRL Science of Quality

About NRL

Accurate, high-quality infectious disease testing protects life, and our way of life, in a connected world.

As an operating division of St Vincent's Institute of Medical Research (SVI), the National (Serology) Reference Laboratory (NRL) supports laboratories and point-of-care sites globally to ensure that the diagnostic and blood screening testing performed to monitor and manage infectious diseases is accurate and effective. We provide consultation and advice on policy related to laboratory testing and deliver services that enhance test quality, creating benefit across the world for individuals and families.

NRL is:

- WHO Collaborating Centre for Diagnostics and Laboratory support for HIV/AIDS and other blood-borne infections
- Accredited by NATA as a Medical Testing Laboratory, compliant with ISO 15189
- Accredited by NATA as a Proficiency Testing Scheme Provider, compliant with ISO 17043
- Certified by BSI for Quality Management, as compliant with ISO 9001
- Licensed by the Therapeutic Goods Administration (TGA) as compliant with the Australian Code of Good Manufacturing Practice

We provide a range of complementary services, including:

- Pre-and post-market evaluations of IVDs and associated sample panels
- Specialised and reference testing services, licensed to cGMP and accredited to ISO 15189
- Biobanking expertise and a significant disease-state plasma repository
- Laboratory capacity and capability building in low- and middle-income countries
- Educational workshops and seminars, mentoring and consultancy
- Global research collaborations

NRL acknowledges the Aboriginal lands on which we live and work, and pays respect to Traditional Owners, Ancestors and Elders.

Contents

Director's Report

With the COVID-19 pandemic continuing throughout 2021, the ability to test with certainty has remained a critical issue for the world. NRL is a global leader in the science of testing for infectious diseases and we strive to ensure the highest standards in every aspect of the testing process.

Formal test kit evaluations were conducted on behalf of the World Health Organization (WHO), Therapeutic Goods Administration (TGA) and commercial test kit manufacturers and have remained a critical service in the pandemic given the limited number of laboratories globally that can perform these kinds of assessments to a regulatory standard. The comparative study of COVID-19 serology test kits, which NRL completed, is published on our website and illustrates a very wide range of performance characteristics. The difference in test performance highlights the value and importance of conducting comprehensive, comparative evaluations for assays released in an emergency setting like a pandemic.

> *At NRL we believe that good science makes all the difference because the outcome impacts everyone.*

Another key area in which NRL has shown innovation and leadership has been the design and provision of quality assurance programs for COVID-19 Rapid Antigen Tests, specifically suited for use in a community-based setting. After continuing to develop our concept throughout the previous year, we were awarded a grant by the Foundation for Innovative and New Diagnostics (FIND) to design, deliver and manage a program including the development of stable, highly characterised samples which can be tested on demand while assessing both the competency of the operator and gaining insights into the performance of the test device itself. The project is targeted towards low- and middle-income countries in the Asian, African and Pacific Island regions and will support data entry of quality assurance results using smartphones in real time. The program will be extended to other analytes and will provide a vital tool in ensuring the effectiveness of point-of-care tests when used outside a laboratory, as occurs routinely across the Western Pacific region.

One significant and positive outcome from the pandemic has been the ability to effectively communicate virtually and securely online. The strengthening of communication technologies has enabled our international collaborations and laboratory capacity building to thrive with impact at greatly reduced cost. Our collaboration with The Mérieux Foundation and Integrated Quality Laboratory Services (IQLS) through the South East Asia Laboratory Strengthening (SEALAB) project was able to pivot quickly and significant progress has been made to strengthen and support laboratory testing through virtual training and one-on-one mentoring in Cambodia and Laos. We acknowledge and thank the Indo-Pacific Centre for Health Security at the Australian Department of Foreign Affairs and Trade for their funding and support. Similarly, we were able to conduct the NRL Workshop on Infectious Diseases virtually in 2021 and we incorporated our Asian Summit because in-person experiences and travel were not possible. The 2021 Workshop was our most successful to date with a rich scientific program, a plethora of international and national speakers and strong international and national participation - all from our homes and across multiple time zones! The video documentary *Testing Times* was created for the event, re-counting COVID-19 experiences from scientific colleagues across the world, and demonstrating NRL's global reach.

This year, NRL supplied our re-formulated External Quality Assurance Schemes for the first time. We have adopted a 'syndromic' panel concept to better support laboratories when analytes are frequently tested together. This approach has simplified our offering and importantly, reduced costs for customers. Our reporting mechanisms have also improved significantly, with graphic presentations, reduced test event reporting timeframes and the provision of annual reports that mine large datasets over a longer time period to identify trends and provide insight into exceptions. We acknowledge and thank our informatics partner One World Accuracy for their support and collaboration with the reporting improvements.

Our Research and Development Team supported a series of collaborative projects regarding HTLV-1. These included the development of a new molecular assay to improve access to this type of test and explore novel collection devices better suited to the extreme temperatures and extended storage periods experienced in remote and very remote Central Australia. We acknowledge and thank all collaborators from Alice Springs Hospital and the Burnet, Doherty, Kirby and Baker Institutes.

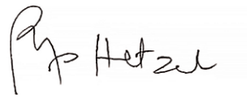
We have continued to improve our quality control products and services with improved functionality in EDCNet™ including the access to customised automated Measurement of Uncertainty reports, which are now available on demand. In addition, a range of laboratory network configuration options were introduced to enable the comparison and display of data across networks of clinical and/or blood screening laboratories. Our quality assurance services to the blood donor screening laboratories of Australian Red Cross Lifeblood are ongoing and we sincerely thank and acknowledge the funding provided by the Australian Government Department of Health.

NRL's dedicated staff and our unique capabilities in test kit evaluation, assay development, laboratory capacity building, validation of testing algorithms and provision of quality assurance products and services have steered our response to the pandemic. I commend and thank staff for the high quality of work, collegiate support and attention to detail shown across every aspect of product and service delivery. We have consistently demonstrated organisational resilience throughout the pandemic with a proactive response to ensure uninterrupted operations and the ongoing provision of both existing and new products and services at full capacity, despite numerous lengthy lockdowns, considerable periods of uncertainty and logistics challenges.

> *NRL is a global leader in the science of testing for infectious diseases and we strive to ensure the highest standards in every aspect of the testing process.*

This report showcases our work throughout 2021 and highlights the key contributions that we've made, despite the ongoing challenges of the pandemic. At NRL we believe that good science makes all the difference because the outcome impacts everyone.

Thank you to our bene-factors , WHO, customers, partners, collaborators and all of our stakeholders. We sincerely appreciate the support we've received from you all!



Dr Philippa Hetzel
MBBS MHA FAICD

Innovative and integrated QC result analysis comparing performance across peer groups.

Laboratories around the world use serology and nucleic acid test kits and instruments to diagnose infectious diseases. Although most test kits are provided to the market under stringent regulatory oversight, unexpected changes in the tests do occur. These changes have the potential to cause false results, to the detriment of patients. By monitoring the performance of the test kits over time, NRL's Quality Control (QC) program provides laboratories with the tools to monitor and detect unacceptable variation, reduce the risk of false patient results and potential harm.

Over the past two decades, NRL has developed unique validated methods for monitoring QC results. Combined, the NRL QC approach is called QConnect™. Our QC scientific staff enable QC manufacturers, DiaMex (Heidelberg, Germany) and TechnoPath Clinical Diagnostics (Ballina, Ireland), to develop QC samples that are optimised to different test kits and do not vary from lot-to-lot. QConnect also incorporates EDCNet™, a world-leading QC informatics platform developed specifically for infectious disease, designed and built by NRL, and is now used by hundreds of laboratories globally. The QConnect™ concept defines acceptance criteria for infectious disease QC test results. It uses the analysis of hundreds of thousands of historic data points submitted to EDCNet by laboratories worldwide over a long period to produce QConnect Limits. This approach ensures the most robust QC analysis for serology and NAT laboratory performance, globally.

NRL staff present the "QConnect Concept" regularly on the world stage in response to requests from laboratories, distributors and test kit manufacturers. Our QConnect approach has driven significant change in the way laboratories think about how QC works in serology and qualitative testing laboratories.

NRL QC SERVICES PROVIDE:

- **Optimised QC reference material,** manufactured by our ISO 13485 certified partners, supplied globally under the Optitrol and Multichem ID brands; co-branded with QConnect
- EDCNet™, NRL's internet-based, peer-reviewed **QC monitoring informatics**
- Scientifically evaluated and validated QConnect™ concept and **QConnect Limits to identify unacceptable QC results**
- **Uncertainty of Measurement reports** based on QC data
- Direct access to NRL's QC **scientific team for scientific support & problem solving**

> *Over the past two decades, NRL has developed unique validated methods for monitoring QC results.*

IMPACT

Automated MU report generation within EDCNet was officially launched in January 2021 and has enabled laboratory staff to download their customised reports on demand. An extended range of laboratory network configuration options has become available to enable comparison and display of data across networks of clinical diagnostic and blood screening laboratories.

Significant progress has been made towards the integration of testing platforms with EDCNet software to support automated uploading of results. This is now available for some platforms, with further expansion planned in 2022. Full integration of all instruments will become accessible in the next few years.

HIGHLIGHTS

In 2021, we introduced a range of changes and new products to support our customers:

- Access to all previous year's reports. New template styles can be created overnight for set-up of new assays
- Launch of the suite of molecular QC samples rebranded as Optitrol™, including blood-borne virus donor screening and viral load products, all following the QConnect concept. This change to our catalogue of products was the culmination of a complex program of work with our manufacturer DiaMex GmbH (Heidelberg, Germany).
- Integration of DiaSorin LIAISON with EDCNet to allow automated uploading of QC data, with more platforms on the horizon.
- An expansion in staffing and resources to support the delivery of world-class QC Services.
- More than 350,000 data points entered across 150+ labs in 20+ countries.

In 2021, significant supply and logistics issues have impacted the availability of some QC samples for Australian laboratories. The patience and understanding of our loyal customers has been greatly appreciated as we have endeavoured to meet supply demands through the complex and challenging circumstances of the pandemic.

External Quality Assessment Schemes

Proficiency programs designed to assess the integrity of tests and testing processes.

NRL External Quality Assessment Schemes (EQAS) are designed to assess the integrity of the entire laboratory testing process for infectious disease markers, from sample receipt through to final interpretation of patient test result. The design and analysis of NRL's EQAS draws upon NRL's extensive experience and scientific methods to ensure maximum scope for error detection. NRL EQAS proficiency panels consist of a combination of positive and negative samples representative of those typically received by a testing laboratory. NRL analyses and reports participants' results online via OASYS — an internet-based application owned and managed by our partner Oneworld Accuracy (1WA) (Vancouver, Canada).

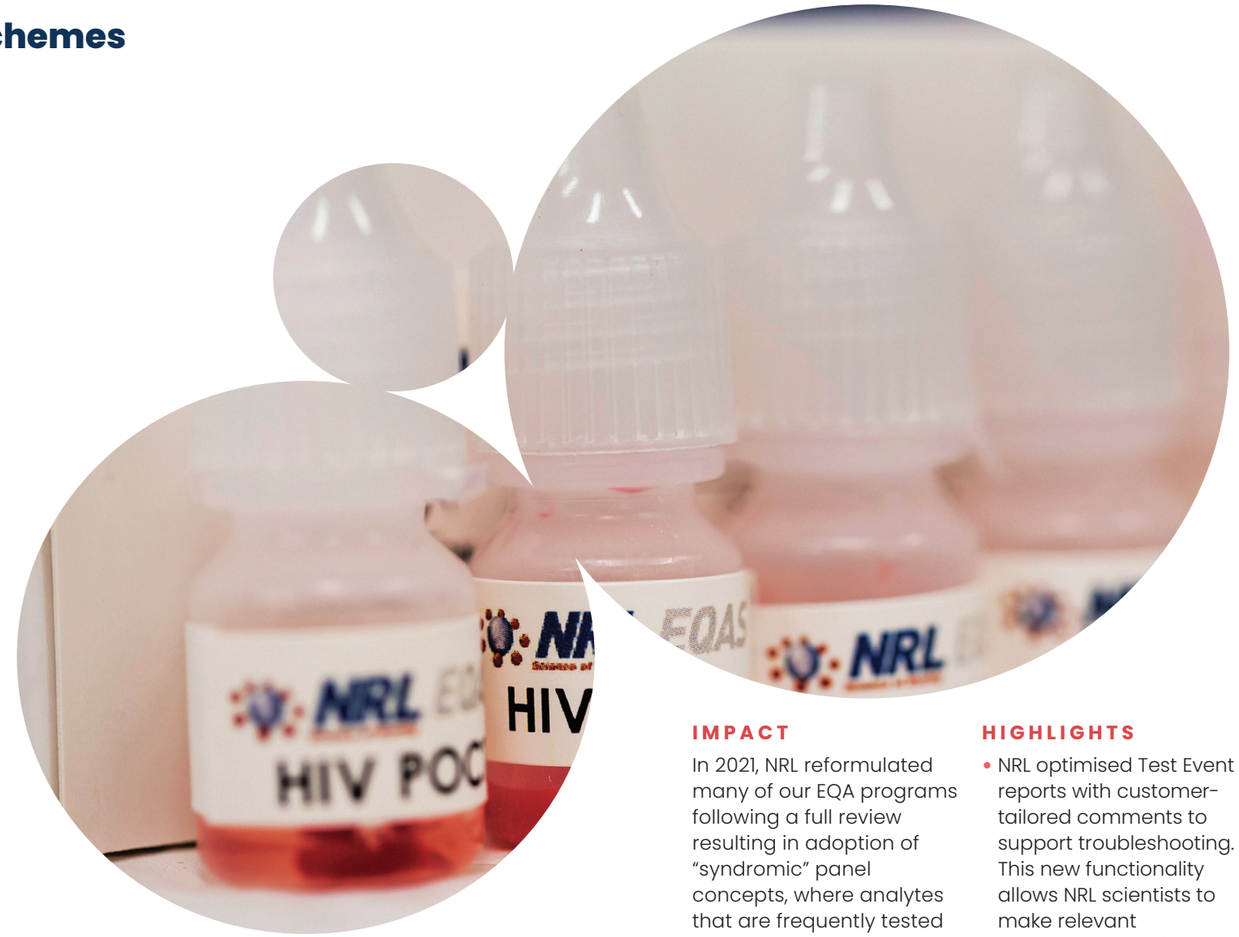
NRL is a fully accredited ISO 17043 provider and our EQAS service includes:

- Genuine and diverse patient samples
- Scientific and technical support to resolve problems in laboratory testing
- A global network of laboratories in more than 50 countries
- Programs designed specifically for clinical and/or blood screening institutions

Participation in EQAS is compulsory in many jurisdictions and is vital in assessing the integrity of the entire infectious disease testing process.

NRL EQAS SERVICES PROVIDE:

- **Real clinical samples** – genetically diverse samples obtained under Material Transfer Agreements. All serology samples are human plasma characterised by NRL's validated testing strategy. Molecular programs contain whole organism or clinical samples. The true status of each sample is known before dispatch.
- **Specific scientific design** – Each test challenge is designed to provide a cross-section of results normally encountered in patient or donor samples and includes positive and negative samples for all analytes over time.
- **Controlled production** – With ISO 17043 accreditation, NRL assures the homogeneity and stability of samples, throughout manufacture, transport and use.
- **Scientific analysis and reporting** - All data submitted to NRL is reviewed for accuracy and reported by NRL scientists. Specific comments are provided on individual laboratory reports and peer data presented in tabular and graphic reports. An annual scientific report analysing the results reported the previous year is provided. Consensus analysis is not practised.
- **Fast turnaround time** – NRL aims to issue all reports within two weeks of each test event deadline, enabling laboratories to take action as quickly as possible when errors are detected.
- **Global networks** – NRL's EQA programs are provided in partnership with 1WA, who provide a secratatiat for a collaboration of many PT providers around the world, all using the same informatics. Many of the PT providers offer NRL-developed programs to their participants, maximising the number of participants across more than 50 countries and expanding the range of technologies being assessed.
- **Integrated informatics software** - Participants submit results online via an internet-based application (OASYS) which supports the enrolment, data entry and management and the automatic reporting of EQA results.
- **Dedicated scientific support** – NRL takes prides in strengthening the relationship between EQAS participants and test kit manufacturers. Our responsibility extends to ensuring your laboratory is reporting accurate test results and our scientists regularly support laboratory-initiated investigations of IVD performance.



IMPACT

In 2021, NRL reformulated many of our EQA programs following a full review resulting in adoption of "syndromic" panel concepts, where analytes that are frequently tested together are included in the same EQA program. For example, NRL now has multiplex panels for hepatitis serology, including all markers for hepatitis A, B, C and D. This approach, apart from reflecting clinical usage, has significantly reduced cost for participants, as they are able to test multiple analytes using the same program.

At request of the WHO South East Asian Regional Office (SEARO), NRL provided a low-cost Multimarker Blood Screening Serology EQAS, to evaluate the performance of 14 central blood transfusion centres in nine SEARO Member States.

HIGHLIGHTS

- NRL optimised Test Event reports with customer-tailored comments to support troubleshooting. This new functionality allows NRL scientists to make relevant laboratory-specific comments in EQAS reports, giving a more personalised experience for participants.
- For the first time, graphic reporting was introduced, to enhance comparisons within and between peer groups. The graphs represent both qualitative and quantitative data analysis, presenting the results in a scientific and intuitive form. In addition, annual reports that summarise and analyse results submitted throughout the year were provided. NRL EQAS collects large amounts of testing data each year, and annual reports mine these datasets to identify trends and exceptions.
- In 2021, NRL released a new respiratory program (RESP435) for Influenza A and B, RSV and SARS-CoV-2 molecular testing. This new program was created in response to the release of new multiplex assays that detect each of these organisms in the same test.
- Logistics is primarily responsible for the shipment of EQAS panels to customers three times per year. In 2021, there were 5,400 panels, dispatched in 567 shipments, to a total about 1,000 customers in 42 countries, each having their own importation regulations. NRL used seven different courier companies and many different airlines to provide transportation into so many countries. In addition to these numbers, NRL logistics sent panels to distributors in 10 countries, accounting for more than 400 additional destinations, where NRL logistics packaged the EQAS so that each site was individually managed in compliance with IATA regulations.

STATS FOR 2021

5,400
Panels dispatched

567
Shipments dispatched

1,000
Customer sites

50
Countries shipped to

7
Courier companies used

1,050
Kilograms of dry ice required for shipments

> *The design and analysis of NRL's EQAS draws upon NRL's extensive experience and scientific methods to ensure maximum scope for error detection.*

Evaluations

Specialised assessments of analytical and clinical performance of IVDs for the detection of infectious diseases.

The advent of SARS-CoV-2 has highlighted the need for comprehensive evaluations of *in vitro* diagnostic devices (IVD) to ensure they meet their stated intended use and conform to key performance, quality and safety criteria. We provided these services to the Australian Therapeutic Goods Administration (TGA), Foundation for Innovative New Diagnostics (FIND), WHO and directly to test kit manufacturers.

A well-designed, laboratory-based assessment of IVD performance can provide a realistic expectation of how the IVD will perform relevant to local conditions, using samples representative of the local population.

As one of 14 WHO Pre-qualification Evaluating Laboratories, NRL is one of only two laboratories authorised to perform pre-qualification assessment of IVDs that detect blood-borne infections. WHO Pre-qualification aims to ensure IVDs for supply to low-income countries are quality-assured, safe, effective and accessible.

NRL Evaluations provide well-characterised clinical samples for use in IVD development and to evaluate the performance of tests, offering customised sample panels to laboratories and manufacturers for verification and/or validation of IVD performance.

> *NRL used its network of partners around the world to collect well-characterised samples of sufficient volume to evaluate over 60 SARS-CoV-2 serology IVDs, giving procurers access to scientifically robust information of test kit performance.*

IMPACT

NRL performed a post-market review of SARS-CoV-2 (COVID-19) serology-based IVDs on behalf of the World Health Organisation. NRL staff developed and maintained syphilis analytical and clinical performance sample panels for use in the performance evaluation of Treponemal and Non-treponemal serology rapid diagnostic tests for WHO prequalification assessments. We also maintained a well-characterised repository of HCV analytical and clinical performance sample panels for the performance evaluation of HCV serology assays for WHO prequalification assessment.

WHO contracted NRL to undertake an evaluation of up to 40 COVID-19 serology test kits using the same specimen panels to independently assess test kit performance and usability to inform potential use in WHO member states. The data generated was used to guide WHO policy on the use of antibody detection tests, including testing algorithms and formulation of procurement requirements. It will also guide future EUL requirements and/or WHO prequalification should COVID-19 diagnostics transition from EUL to the full pre-qualification portfolio.

NRL performed a comparative evaluation of antibody detection tests against a well-characterised panel of COVID-19 seropositive, seronegative, cross reacting and interfering substances specimens. As a result of this study, manufacturers of COVID-19 serology test kit evaluations were able to acquire meaningful and scientifically sound performance data that can aid in supporting the applicability of their test kit for the intended use. In total, 35 assays (9 EIAs and 26 point-of-care tests) were evaluated and individual tailored reports issued to each manufacturer and also published via the NRL website. The variation in assay performance observed, highlights the need for comprehensive evaluation of assay performance, particularly for assays released onto the market in an emergency setting.

Post-market review of SARS-CoV-2 (COVID-19) serology-based IVDs were contracted by 10 (national and international) commercial manufacturers to assess kit performance of SARS-CoV-2 serology test kits.

- The same set of well-characterised samples (COVID-19 seropositive, seronegative, cross-reacting, interfering substances) were tested on 16 test kits across a number of different platforms
- NRL analysed all of the results and published individual reports for each assay reviewed on the NRL website
- The study demonstrated a wide range of performance characteristics of Anti-SARS-CoV-2 assays and highlighted the value in comprehensive, comparative testing of assay performance.

HIGHLIGHTS

- Joining the global fight against the COVID-19 pandemic by evaluating assays that detect Anti-SARS-CoV-2. Early in the pandemic, it became obvious that the large numbers of IVDs for SARS-CoV-2 had a range of performance characteristics. There were obvious and well-reported failures of test kits across the globe. Most regulatory authorities removed the stringent regulatory criteria used for other infectious disease testing and allowed SARS-CoV-2 test kits be accessed under Emergency Use Listings. This facilitated immediate access by laboratories in the fight against the disease, however, it did remove evidence-based selection of tests. In response to this situation, NRL used its network of partners around the world to collect well-characterised samples of sufficient volume to evaluate over 60 SARS-CoV-2 serology IVDs, giving procurers access to scientifically robust information of test kit performance.

SERVICES DELIVERED

35
Post-market Anti-SARS-CoV-2 Serology Test Kits assessments on behalf of WHO

16
COVID-19 Serology Test Kits reviewed as part of a post-market anti-SARS-CoV-2 test kit study for 10 Independent IVD manufacturers

2
Laboratory Performance Evaluation of Syphilis serology assays for WHO Prequalification

1
Laboratory Performance Evaluation of an HCV Molecular Assay for WHO Prequalification

Testing Services

A range of validated services, including TGA-licensed blood and tissue donor screening for HIV, HBV, HCV, HTLV and syphilis from both living and cadaver donors.

Utilising validated testing algorithms, NRL Testing operates as a reference laboratory for HIV, HCV and HTLV specimens whose status cannot be resolved by routine screening in diagnostic laboratories. Where IVDs are not validated for alternative specimen types, NRL Testing offers TGA-licensed testing of specimens for use in certain serology and molecular IVDs under the TGA Authorised Prescriber Scheme.

NRL Testing undertakes contract testing for scientific projects in collaboration with other organisations for a range of services that include:

- Development of new assays
- Validation of testing algorithms
- Epidemiological studies
- Stability studies (Accelerated and Long-term stability)

In addition, NRL Testing offers batch-release testing of HIV and syphilis rapid IVDs for Victorian point-of-care testing sites. Batch release testing involves testing of new batches of IVDs to confirm that their performance is consistent from one batch to another.

NRL has verified the suitability of tissues and organs for transplantation and provided certainty for blood and tissue/organ donors...

IMPACT

The contribution of testing services has verified the suitability of tissues and organs for transplantation and provided certainty for blood and tissue/ organ donors regarding the outcome of initially reactive screening tests.

HIGHLIGHTS

- Provision of TGA-licensed screening of specimens collected from living and cadaver blood and tissue donors, reference testing, and contract testing for projects
- Re-implementation the DiaSorin LIAISON XL MUREX HBsAg Quant CLIA and DiaSorin LIAISON Treponema Screen CLIA testing for donor screening and diagnostic testing
- Performance verification of the MP Diagnostics HTLV I/II EIA for the detection of anti-HTLV-I/II antibodies ahead of use in a HTLV Longitudinal Study administered by the Baker Heart and Diabetes Institute
- Performance verification of the DiaSorin LIAISON SARS-CoV-2 S1/S2 IgG assay for sample characterisation and external quality assessment reference testing
- Performance verification of the WANTAI SARS-CoV-2 Ab ELISA assay and the Cepheid Xpert Xpress SARS-CoV-2 assay for sample characterisation and external quality assessment reference testing

STATS FOR 2021

6,086
Screening tests conducted

1,620
Reference tests conducted

4,026
Internal testing (sample characterisation and OR Reference testing) conducted

49
Tests conducted as part of collaborative Longitudinal study projects

721
Proficiency tests conducted

Training and Consulting Services

Services which are culturally sensitive and customised to locally identified needs.

NRL works in collaboration with Ministries of Health, laboratories and in-country development partners to ensure that our international capacity-building activities are relevant and support appropriate, sustainable and effective outcomes. As a WHO Collaborating Centre for Diagnostics & Laboratory Support for HIV/AIDS and other blood-borne infections, NRL staff have significant expertise and are highly regarded as consultants and technical experts by Ministries of Health, non-government agencies and WHO. NRL staff also support the development of technical guidance, and make recommendations in line with national and international strategies.

> *NRL staff have significant expertise and are highly regarded as consultants and technical experts by Ministries of Health, non-government agencies and WHO.*

IMPACT

NRL continued its support for WHO and countries across the Western Pacific and South-East Asian regions, including as a WHO Collaborating Centre for Diagnostics & Laboratory Support for HIV/AIDS and other blood-borne infections, through a range of activities such as:

- Supporting WHO regional offices with WHO technical workshops by delivering presentations, chairing and participating in panel sessions on various topics relating to the quality of testing and quality assurance programs.
- Providing technical expertise at the request of WHO WPRO, and participating in a Mock Review of the preparation for an effectiveness audit of the Elimination of Mother-To-Child-Transmission (EMTCT) of HIV and syphilis in Cambodia, from June to Sept 2021.
- Hosting a series of virtual seminars, covering topics relating to: quality assurance, monitoring assay and testing proficiency through EQAS and Quality Control; quality management systems of testing services for WHO priority diseases such as HIV, hepatitis B and hepatitis C and syphilis.
- In collaboration with the WHO Incidents and Substandard/ Falsified Medical Products Team Regulation and Prequalification Department, NRL drafted a white paper for publication in a peer-reviewed journal. NRL continues to actively develop PoCT QA programs based on this work.
- As a member of the Executive Committee of the Australian Network of WHO Collaborating Centres, NRL is involved in activities aimed at promoting WHO work and connecting Australian WHO Collaborating Centres to make collaborations more effective.
- Throughout 2021, NRL staff provided ongoing expert advice to WHO regarding test kit evaluations protocols, testing algorithms, technical aspects of laboratory testing and quality management. NRL takes great pride in its support of WHO activities globally.

HIGHLIGHTS

- NRL continued its collaboration with The Mérieux Foundation and Integrated Quality Laboratory Services (IQLS) through the South East Asia Laboratory Strengthening (SEALAB) project. Commissioned and funded by the Indo-Pacific Centre for Health Security at the Australian Department of Foreign Affairs and Trade, SEALAB aims to reinforce national health systems in Cambodia and Laos by strengthening both human and animal laboratory capacity to detect and respond to emerging infectious disease outbreaks, which are potentially pandemic and/or zoonotic threats. NRL's role in SEALAB is to assess capacity and deliver training and mentoring to strengthen the quality of testing performed in human health laboratories. NRL responded to the challenges of the COVID-19 pandemic by delivering our programs virtually from Australia, through training workshops and one-on-one mentoring sessions. This approach has proved to be a very successful model, despite some initial language barriers and technical difficulties. The low-cost nature of virtual training has enabled NRL to mentor each laboratory individually on a frequent and regular basis, which has, in turn, strengthened in-country relationships and partnerships.
- In collaboration with Austin Health and the Royal College of Pathologists of Australasia (RCPA), NRL launched a one-day virtual training workshop focusing on quality requirements for Australian pathology laboratories performing infectious diseases testing. The training workshop introduced and reviewed relevant quality requirements for medical microbiology laboratory testing that inform clinical decision-making, diagnosis and support effective patient outcomes. Initially targeted at hospital-based microbiology across Victoria, this training will be continued annually and expanded in reach to include all pathology disciplines across Australia.
- NRL staff delivered 40 training events, including 130 hours of web conferencing, to 270 participants throughout the year.

Research and Development

Translating new ideas and products from the research laboratory to the market.

Organisations enabling research translation are uncommon in academia because we focus on the "Development" aspects of R & D rather than breakthrough or discovery research.

NRL has considerable expertise in regulatory affairs from many years of working with the TGA, and operates under a mature Quality Management System. Together with our expert knowledge in diagnostics and laboratory medicine, NRL is well-placed to assist in the formal design of new IVDs and to expedite the translation of existing design concepts into commercially-ready products and services. This includes the provision of external laboratory support to verify and validate that a new IVD is fit-for-purpose, and to support sample processing and testing for clinical trials.

While historically, we have specialised in blood-borne infectious disease diagnostic testing, NRL's skills and expertise can be applied to testing for other infectious pathogens, and indeed beyond the infectious disease research space. Furthermore, our partnerships and collaborations with QC/device manufacturers and other commercial/pharmaceutical partners extend globally and strengthen our relationships and expertise.

In addition to providing customised research-related services, NRL has an active in-house research program with a current focus on the development of novel IVDs aimed at improving the quality, accessibility and breadth of tests available to patients living in regional, remote and very remote areas.

IMPACT

NRL has continued its advocacy for the application of quality processes at all levels of diagnostic testing. With the widespread implementation of SARS-CoV-2 Antigen Rapid Diagnostic Tests (RDT) globally – including in community settings like airports, schools, and workplaces – we focused on innovative solutions to ensure the quality of that testing. Often, these community sites were checkpoints, preventing transmission by identifying infectious individuals. NRL was awarded a grant by FIND under the ACT-A project (https://www.act-a.org/) to design, deliver and manage a SARS-CoV-2 Antigen RDT Quality Assurance (QA) program. This includes the development of stable, highly-characterised samples, the provision of Competency and External Quality Assessment Panels and the development of smartphone data entry for QA results. The QA program is targeted towards low- and middle-income countries in the Asian, African and Pacific Island regions.

Our R&D team is a stand-alone department that also supports research and development activities across NRL's departments including EQAS, QC, Evaluations and Testing teams.

In 2021, we said goodbye to Prof Rose Ffrench, Executive Manager of Clinical and Research Services, and we wish her all the best in her retirement. Prior to Rose's departure, we were pleased to recruit Dr Nick Vandegraaff as a Senior Scientist into the Research team. Nick is a virologist with a strong academic background and considerable experience in commercial IVD development in Australia. He has continued to lead NRL's R&D assay development program.

> *NRL is well-placed to assist in the formal design of new IVDs and to expedite the translation of existing design concepts into commercially-ready products and services.*

HIGHLIGHTS

- In 2015, the WHO set global targets for the elimination of hepatitis C virus (HCV) by 2030. To progress this aim, the Australian Government granted funding to the Kirby Institute (University of NSW) and the International Centre for Point-of-Care Testing (Flinders University) to scale up the use of HCV PoCT in high prevalence areas such as needle and syringe exchange sites and prisons (https://hepcpoct.com.au/). NRL's role in this study is to design, implement and co-manage the HCV PoCT QA program. This consists of the provision of Competency and External Quality Assessment Panels using a novel, dried, whole blood sample type. The study is expected to continue through to 2024.
- 2021 saw the successful completion of a collaborative study with the Burnet Institute that used a Western Blot technique, developed at NRL, to assess the progression of different COVID-19 antibody isotype responses over time; including IgM, IgG and IgA and subclasses. This method differentiated the proteins to which patients were responding over time to SARS-CoV-2 and was used to guide further development activities at the Burnet for a rapid point-of-care test targeting dimeric IgA in patient serum post-infection.
- NRL is also involved in ongoing research focused on developing new molecular assays that will strengthen the NRL testing menu for Human T cell Leukaemia Virus Type 1 (HTLV-1), a blood-borne infectious pathogen known to disproportionately affect populations of Indigenous Australians in Central Australia. In collaboration with Alice Springs Hospital and the Burnet and Doherty Institutes, these new tests are being co-developed for use with novel specimen collection devices that are suited to sample collection and storage over extended periods in remote and very remote settings. Funding was successfully obtained from the Australian Centre for HIV and Hepatitis Virology Research (ACH2) to support this work, and the preliminary data has been presented at multiple national meetings including the 2021 ACMD Research week, Australian Institute of Medical and Clinical Scientists (AIMS) National Scientific Meeting as well as the annual ACH2 and NRL workshops.
- With the successful development of the new HTLV molecular assay, the NRL Research and Testing teams have together been able to provide a comprehensive range of testing services for a five-year longitudinal study led by the Baker Institute aimed at establishing associations of HTLV-1 infection with disease among Aboriginal people living in Central Australia. Participant recruitment for this study commenced in late-2021 and NRL is coordinating with Baker and Kirby Institute staff, Indigenous health services and regional pathology centres to ensure samples are collected, transported, processed, tested and reported in a timely manner.
- The R&D team continues to support national collaborators such as the Burnet, Doherty, Baker and Kirby Institutes, researchers at Alice Springs Hospital and Flinders University, as well as international collaborators in the World Health Organisation's (WHO) Western Pacific and South-East Asian regions and the Foundation for Innovative New Diagnostics (FIND).

SVI Biobank

Extensive human biospecimen repository and validated sample processing services.

The SVI Biobank is managed by, and housed at, NRL's primary laboratory facility. The Biobank is a storage resource and repository for research groups, clinical trials organisations and others requiring contract storage of biological samples. We cater to researchers and clinical research organisations, providing the facility to acquire, process, and store samples of any disease type. Our repository consists of a variety of human biospecimen types such as whole blood, plasma, serum, urine, stool, and tissue. Our specimens are derived from patients with a diverse range of diseases, including type 1 diabetes, cancer, hepatitis and other infectious diseases.

With significant expertise in quality management systems and accreditation, NRL is well-placed to deliver biobanking and related services to support clinical trials and clinical and other research projects across the St Vincent's Hospital Melbourne campus and beyond.

IMPACT

Biobanking is being provided to SVI's BANDIT clinical trial for type 1 diabetes, which aims to slow or stop progress of the disease in newly diagnosed people. The trial is being run across four hospitals in Melbourne and Adelaide, recruiting patients recently diagnosed to receive the trial drug (or placebo).

Six blood samples are being collected over the two-year trial period. Biobank is processing four different sample types from the donated blood and will store them securely until the end of the trial, when samples from each donor will be tested together, to evaluate results.

> *We cater to researchers and clinical research organisations, providing the facility to acquire, process, and store samples of any disease type.*

HIGHLIGHTS

- Biobank participated in an external Quality Assurance Program (QAP) for processing and cryopreservation of peripheral blood mononuclear cells from human whole blood. This is one of Biobank's core processes. The QAP was facilitated by the Immunovirology Research Network of Australia. Biobank met the performance standards of the QAP and was certified as competent in this procedure in January 2021.
- In May, Biobank commenced support of the DARWIN study in collaboration with the Gastroenterology Department at St Vincent's Hospital Melbourne. This study aims to determine the effect of diet on appetite regulation, weight, and steatosis in individuals with Non-alcoholic Fatty Liver Disease. The project comprises two trials: one comparing the effects of two different diets in participants, and the second observing the effects of bariatric surgery on progression of the disease. Repeat samples (six visits) from a total of 45 patients from across both studies will be processed and stored at Biobank.
- Biobank received a substantial boost to our sample collection in August, when we became the custodians for an extensive collection of biospecimens previously collected from patients with cardiovascular disease – the Melbourne Vascular Tissue Repository. Samples were collected from 2008 onwards, from approximately 500 total participants across three research projects run by the SVHM Cardiology Department. Complementary clinical data and patient questionnaires were also obtained in support of this resource. Biobank will manage the secure storage, inventory, and release of these biospecimens for future research.
- The Victorian Pancreatic Cancer Biobank (VPCB) aims to build a collection of biospecimens from pancreatic cancer patients undergoing treatment at various hospital sites across Victoria and is housed at Monash University. In October, Biobank became the SVHM hub for the VPCB. Biospecimens from any participants in the VPCB who are treated at SVHM come to Biobank for initial processing and storage, prior to bulk shipment to the central site at Monash University for long-term storage.

STATS FOR 2021

310
New participants recruited

630
Participant samples acquired

7,854
Sample vials stored

Workshops

Delivering state-of-the-art professional development for medical scientists and pathologists.

In 2021, NRL conducted our 37th Annual Workshop on Infectious Disease, in association with an Asian Summit component from 11-13 October as a virtual experience. Because the workshop was held virtually, NRL was able to invite many international keynote speakers of exceptional quality, as well as presenters from across Australia.

The conference included a focus on COVID-19, and we were fortunate to have both Professor Hans Zaaijer and Professor Anton Van Weert from the Netherlands discuss the Dutch response to COVID-19. Both were in the forefront, supporting local Dutch and European Ministries of Health. Professor Ben Cowie in his seconded role as Victoria's Deputy Chief Health Officer, provided an overview of the Australian response and a range of speakers from across Australia discussed the challenges faced in responding to the pandemic. One of the most unique and exciting sessions was *Testing Times*, a one-hour documentary created by NRL in which laboratory scientists from across the globe were interviewed on the immediate effect of COVID-19, how their country responded and the personal impact of the virus on themselves and colleagues. Both enlightening and poignant, the video can be viewed at https://www.nrlquality.org.au/testing-times-2021-a-documentary

While point-of-care testing has become commonplace in Australia due to the widespread use of COVID-19 rapid antigen testing, unlike overseas, this kind of testing for hepatitis C virus, HIV and sexually transmitted infections has been slow to be adopted. NRL has collaborated with the Kirby Institute (University of New South Wales) and Flinders University to provide quality assurance programs to support their point-of-care activities in Central Australia. In collaboration with these two organisations, one conference session explored the impact, barriers and opportunities of point-of-care testing in Australia, including speakers from the Australian Department of Health and NATA, as well as implementors and test users from Central Australia.

The virtual integrated Australian and Asian Workshops were well received and attended, with a strong scientific program receiving excellent reviews. We acknowledge and thank our industry sponsors and partners for the event – without their support, the workshops could not be conducted.

> *One of the most unique and exciting sessions was Testing Times, a one-hour documentary created by NRL in which laboratory scientists from across the globe were interviewed on the immediate effect of COVID-19, how their country responded and the personal impact of the virus on themselves and colleagues.*

Scan QR code to view documentary

Publications & Presentations

PRESENTATIONS:

Quality Control of Qualitative Testing of SARS-CoV-2 in Clinical Laboratories
In: Critical role of clinical laboratories in the COVID-19 pandemic, Educational Workshop at the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Virtual Event
Joe Vincini and **Wayne Dimech**

Monitoring and Evaluation Frameworks for Diagnostics
International Atomic Energy Commission and World Health Organisation – SEARO Webinar Series to support the COVID-19 testing laboratories in the Asia and the Pacific Region, 9 November 2021
Wayne Dimech

The Complexity of Infectious Disease Testing
Abbott Transfusion Medicine Health Institute
Wayne Dimech

Experience in Using the WHO IS and Development of Secondary Standards
WHO Two Days Webinar on use of WHO international reference materials for in vitro diagnostics (IVDs) and production of secondary standards, 11-12 February 2021
Wayne Dimech

Evaluating SARS-CoV-2 testing devices SoGAT SARS-CoV-2
Workshop Agenda, National Institute of Biological Standards and Controls, 10–11 June 2021
Wayne Dimech

Maintaining the Quality of Testing in a Pandemic
Saal Foley Lecture Australian Institute of Medical Scientists – NSM Conference
Wayne Dimech

Quality Control in TTI Laboratory
Asian Association of Transfusion Medicine, Quality Assurance Program in Transfusion Transmissible Infection Testing WHO – Online Pilot Training Program in Association with Asian Association of Transfusion Medicine
Sandy Walker and **Wayne Dimech**

The Standardisation and control of infectious disease testing
Laboratory Management Conference, MEDLAB, Dubai, June 2021
Wayne Dimech
Bringing Quality Assurance Programs for Infectious Disease Testing to Point-of-Care
37th NRL Workshop on Infectious Disease Testing, October 2021
Liza Cabuang

Sample Collection in Remote Settings for HTLV-1 testing
37th NRL Workshop on Infectious Disease Testing October 2021
Nick Vandegraaff

COVID Serology Evaluations
37th NRL Workshop on Infectious Disease Testing October 2021
Wayne Dimech

PUBLICATIONS

Johnson P & **Cabuang L**. Proficiency Testing and Ring Trials. Rev. Sci. Tech. Off. Int. Epiz., 2021, 40 (1), 189-203

Hong X; Luckenbaugh L; Mendenhall M; Walsh R; **Cabuang L**; Soppe S; Revill P; Burdette D; Feierbach B; Delaney W; Hu J. Characterization of Hepatitis B Precore/Core-Related Antigens. J. Virol. 2021. Jan 13;95 (3)

Wayne Dimech. The Standardization and Control of Serology and Nucleic Acid Testing for Infectious Diseases. Journal of Clinical Microbiology Reviews. Volume 34 Issue 4 (2021) e00035-21

Ngoc Minh Hien Phan, Helen M. Faddy, Robert L. Flower, **Wayne J. Dimech**, Kirsten M. Spann and Eileen V. Roulis. Low Genetic Diversity of Hepatitis B Virus Surface Gene amongst Australian Blood Donors. Viruses. 2021, 13, 1275. doi:10.3390/v13071275

Global Reach

WE ACKNOWLEDGE AND THANK OUR STAKEHOLDERS

- Abacus dx
- Abbott Diagnostics
- Aikenhead Centre for Medical Discovery
- Alice Springs Hospital
- AusDiagnostics
- Australian Centre for HIV and Hepatitis Virology Research (ACH2)
- Australian Global Health Alliance
- Australian Government Department of Health
- Australian Institute for Medical and Clinical Scientists
- Red Cross Lifeblood
- Australasian Society for HIV, Hepatitis & Sexual Health Medicine
- Australian WHO Collaborating Centre Network
- Austin Health
- Baker Institute
- Becton Dickinson
- Biomerieux
- Bio-Rad Laboratories Pty Ltd
- BD Life Sciences Blood and Tissue Donation Services
- Burnet Institute
- Bureau of Medical Laboratory Services (BMLS), Ministry of Health, Cambodia
- Cepheid
- CSL Behring Australia
- Department of Health and Human Services, Victoria
- DiaMex GmbH
- DiaSorin Australia Pty Ltd
- Flinders University International Centre for Point-of-Care Testing
- Foundation for Innovative New Diagnostics
- Genetic Signatures
- GreenLight Clinical
- Hologic
- Immuno-Virology Research Network (IVRN)
- Indo-Pacific Centre for Health Security
- Integrated Quality Laboratory Services (IQLS)
- Infectious diseases testing laboratories
- Institutions providing samples for NRL programs
- International Plasma and Fractionation Association
- Irish Blood Transfusion Service
- IVD Manufacturers
- Kirby Institute
- LGC
- MNX Global Logistics
- MP Biomedicals Australasia Pty Ltd
- National Association of Testing Authorities, Australia
- National Reference Laboratory/San Lazaro Hospital STD AIDS Cooperative Central Laboratory, Philippines
- New South Wales Ministry of Health
- New Zealand Blood Service
- Oneworld Accuracy, Canada
- Ortho-Clinical Diagnostics
- Pathology Technology Australia
- Peter Doherty Institute for Infection and Immunity
- PRONTO!
- QIAGEN
- Research Institute for Tropical Medicine, Philippines
- Roche Diagnostics Australia
- Royal College of Pathologists of Australasia (RCPA)
- Shanghai Blood Centre
- Siemens Healthineers
- South African National Blood Service
- SpeeDx
- St Vincent's Hospital Melbourne
- St Vincent's Hospital Sydney
- Sysmex
- Technopath Clinical Diagnostics
- The Mérieux Foundation (FM)
- Therapeutic Goods Administration
- US Centres for Disease Control and Prevention
- Victorian Infectious Diseases Reference Laboratory
- Vircell
- World Health Organization Headquarters and Regional Offices
- World Health Organization Member States
- Yayasan KNCV Indonesia

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MEDICAL RESEARCH

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