2020 NRL YEAR

SVI
ST VINCENT'S INSTITUTE
MEDICAL RESEARCH

NRL

ABOUT NRL

NRL specialises in the science of quality by monitoring the performance of tests and testing for infectious diseases.

As an operating division of St Vincent's Institute of Medical Research, 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 the quality of the testing being performed.

A WHO Collaborating Centre for Diagnostics and Laboratory support for HIV/AIDS and other blood-borne infections, accredited to ISO 15489 as a Medical Testing Laboratory, ISO 17043 as a Proficiency Test Scheme Provider and licensed by the Therapeutic Goods Administration (TGA) as compliant with the Australian Code of Good Manufacturing Practice, NRL provides a range of complementary services:

- Highly sophisticated quality assurance program (quality control samples and monitoring software; international proficiency testing programs to 2000+ laboratories in 70+ countries)
- Pre-and post-market evaluations of IVDs and associated sample panels
- Specialised and reference testing services, licenced to cGMP
- Biobanking expertise and a significant disease-state plasma bank
- Laboratory capacity and capability building in lower and middle income countries
- Educational workshops and seminars, mentoring and consultancy and
- Global research collaborations

CONTENTS

SVI acknowledges the Aboriginal lands on which we live and work, and pays respect to Traditional Owners, ancestors and elders.

DIRECTOR'S REPORT

The COVID19 pandemic changed the world in 2020 and highlighted that infectious disease, like war, can bring the world to a standstill. It has exposed how connected and interdependent we all are – across global, as well as local communities. In this modern world, our welfare depends on keeping all of us healthy. Keys to controlling the spread of infectious diseases and any future pandemics is establishing state of the art testing in both the developed and developing world.

What our connected world needs is the ability to test with certainty. NRL is a global leader in the science of testing for infectious diseases and we strive to support laboratories to ensure that the highest standards exist in every aspect of the testing process. We have continued this tradition through our pro-active response to SARS-CoV-2 and I am proud to report, we continued to operate uninterrupted and provide both existing and new products and services at full capacity despite numerous lockdowns and uncertainty. NRL's unique capabilities in assay development, test kit evaluation, validation of testing algorithms and provision of quality assurance products and services steered our response to the pandemic to support laboratories to maintain the accuracy of pathology testing.

One of our key contributions throughout the pandemic has been our support for WHO with the development of protocols for the formal evaluation of SARS-CoV-2 serology test kits, also known as In-vitro diagnostic devices (IVD) and subsequently, the formal evaluation of SARS-CoV-2 serology tests on behalf of WHO. When new infections emerge and tests are rapidly developed, the usual regulatory controls are challenged and the accuracy of testing less certain. In countries where regulatory frameworks do not exist, the WHO Emergency Listing is a critical initiative to support ministries of health, funding bodies and laboratories in their choice of IVDs. We have formally evaluated a series of new Point of Care (POCT) IVD test kits for SARS-CoV-2 serology on behalf of WHO. These rapid tests are an essential tool for urban and especially remote communities to be able to test and diagnose COVID19 quickly and accurately. We have also supported the Doherty Institute and Therapeutic Goods Administration (TGA) with evaluations of rapid serology test kits for use in Australia and partnered with Pathology Technology Australia and test kit manufacturers to provide this evaluation service directly.

A repository of serum, plasma and peripheral blood mononuclear cells from SARS-CoV-2 infected donors was established including both cross-reacting and seroconversion samples. Subsequently, a very large COVID19 plasma repository of well-characterised samples was established with the support of our QC manufacturing partners Technopath Clinical Diagnostics and DiaMex GmbH. This resource has

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enabled our EQAS and IVD Evaluations programs to flourish.

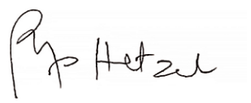
Our Testing services team enabled a tertiary healthcare service in Melbourne to accelerate and expand their testing capacity and capability through providing staff training and physical access to our testing platform while theirs was being installed and commissioned. This happened at a crucial time early in the pandemic when state testing services were severely pressured.

Our existing HIV collaboration with the National Measurement Institute (NMI), the Australian Government national authority on measurement, pivoted to create an Australian standard for SARS-CoV-2 RNA. Using inactivated virus obtained from Doherty Institute under Material Transfer Agreement, NMI created dilution series which were verified by collaborators. The project created both a national standard, as well as additional reference standards used to calibrate and validate molecular assays.

NRL also collaborated with Burnet Institute and Doherty Institute on a Victorian Government initiative to develop novel serology tests for COVID19 to monitor the development and waning of antibody responses to SARS-CoV-2. Our colleagues at the Burnet have developed an immunoassay and rapid POCT for the development of dimeric IgA in patient serum post infection. NRL established a western blot assay to assess the development of antibody responses of different isotypes over time, including IgM, IgG and IgA and subclasses in order to differentiate the proteins to which a person is responding. We aim to have a definitive reference testing algorithm established.

And, as part of the reformulation of our EQAS, we established a novel respiratory scheme containing the SARS-CoV-2 virus to assist pathology laboratories in ensuring their molecular testing of suspected COVID patients is accurate and will ensure that rates of false positive and false negative test results are minimized. We also supported customers by providing a new range of SARS-CoV-2 quality control molecular and serology products from our QC manufacturing partners, expanding our already comprehensive QC menu.

Certainly, 2020 was a challenge for us all and the end of the pandemic is not yet in sight. I extend my thanks to the Australian and Victorian Governments for funding support, our customers for their loyalty, our partners, collaborators and all our stakeholders for your support of our work and mission. Together we have significantly improved the quality and accuracy of testing globally!



QUALITY CONTROL

Comprehensive QC programs ensure the patient test results are as accurate as possible, reducing the risk of false positives or negative test results.

EDCNet and QConnect are an Australian success story.

Some of the world's largest companies provide serology and nucleic acid test kits and instruments used to diagnose infectious diseases. The external quality assurance of these instrument and test kits is a critical component to their use. External Quality Control (QC) programs require the highest quality reference materials supported by scientifically sound analysis and powerful informatics.

EDCNet™, a world-leading QC informatics platforms developed specifically for infectious disease, was designed and built by NRL and is now used by hundreds of laboratories globally. QConnect™ is a concept developed by NRL to establish acceptance criteria for infectious disease QC test results. It utilises novel and robust analysis systems to produce QConnect Limits, which ensures the laboratory QC test data sets are analysed using thousands of peer data points. This approach ensures the most robust QC analysis for serology and NAT laboratory performance globally. EDCNet and QConnect are an Australian success story.

NRL QC SERVICES PROVIDE:

- Optimised QC reference material, manufactured by our ISO13485 certified partners, supplied globally under the Optitrol and Multicehm ID brands; co-branded with QConnect
- Cloud-based, peer-reviewed QC monitoring informatics, EDCNet
- Scientifically evaluated and validated QConnect concept and QConnect Limits to identify unacceptable QC results
- Direct access to NRL's QC scientific team for scientific support & problem solving

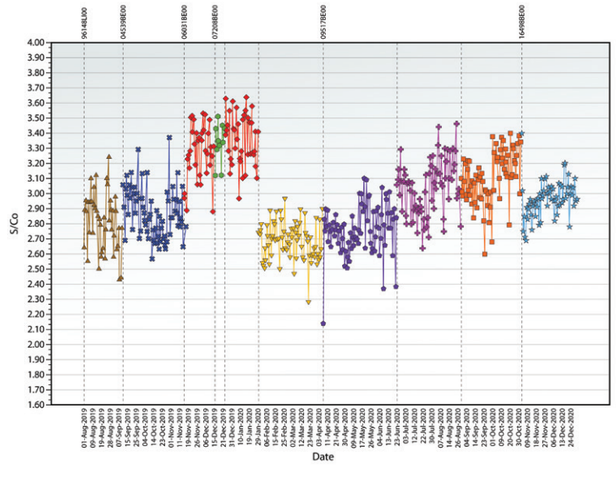


Chart: *QC results plotted in EDCNet showing variability between reagent lots*

EDCNet

QConnect
Follow the trend

NRL responded early to the emerging need for SARS-CoV2 QCs in 2020, offering serology & NAT QCs to the Australasian market.

IMPACT

In 2020, major steps were taken to further consolidate the NRL QC program by automating the generation of MU reports within EDCNet so that they are now available on demand within the software. A range of laboratory Network options are also available to enable comparison and display of data. Significant progress has been made towards the integration of testing platforms with the software to support uploading of results which will become available in 2021.

HIGHLIGHTS

In 2020, we introduced a range of changes and new products to support our customers:

- Automated MU reports were developed in readiness for the new reporting year. MU reporting is now on demand and fully integrated into EDCNet with access provided to reports from all previous years.
- EDCNet Networking options improved and expanded to four new displays – Distributor, QC Manufacturer, Assay Manufacturer, and Laboratory Networks.
- Rebranding of the QConnect range of QC sample as Optitrol™, while being co-branded with QConnect, signifying the samples as being appropriate for the QConnect concept. This change of branding for both the serology and nucleic acid test QCs has aligned our brands with those of our supplier Diamex GmbH (Heidelberg, Germany).
- The rapid spread of SARS-CoV-2 in 2020 saw the need for new high quality molecular and serology QCs to monitor the new COVID test kits released by the IVD manufacturers. Early in 2020, NRL provided SARS-CoV-2 QCs, which includes the molecular Optitrol NAT SAR-CoV-2 and the serology anti-COVID-19 IgG and anti-COVID-19 IgM products, to the Australian market.
- 340K plus data points entered across 140+ labs in 19 countries.

SVI BIOBANK

The SVI Biobank has been established to enable faster translation of research ideas into discoveries by creating a repository of well-credentialled samples that are already available on the St Vincent's Hospital Melbourne campus.

It is a storage resource and sample repository for the use of research groups, clinical trials organisations, and others requiring contract storage of biological samples. We cater to researchers and Clinical Research Organisations (CROs), providing access to facilities to store samples of any disease type and hold a variety of human specimen types such as whole blood, plasma, serum and tissue in the repository. Our specimens are derived from patients with a diverse range of diseases, including diabetes, cancer, hepatitis, and other acute and chronic diseases, and are available to all researchers as an immediate resource to support their work.

With our significant strengths in the application of quality management systems and quality assurance, NRL is well placed to provide SVI's biobanking services.

IMPACT

With our significant strengths in the application of quality management systems and quality assurance, NRL is well placed to provide SVI's biobanking services. The SVI Biobank is now certified by the Immunovirology Network (IVRN) as competent in the processing of PBMC, and all of our biobank staff participate in this ongoing quality assurance program. As a facility of the NRL, the SVI Biobank works within the ISO 9001 quality framework, and is supported by a quality management system, and staffed specimen reception. Biobank's freezers and fridges are continuously temperature monitored and recorded 24-7. Together, these processes ensure robust sample handling protocols and confidence in chain-of-custody and storage of samples for our users.

In 2021, NATA will for the first time offer a Biobanking accreditation program - ISO 20387. NRL will attain this accreditation in 2021 by building on our extensive quality management systems and assurance programs. Accreditation under this program provides consumer confidence in our protocols and services by ensuring consistent service excellence in samples banked and stored.

Helen Macpherson Smith Trust

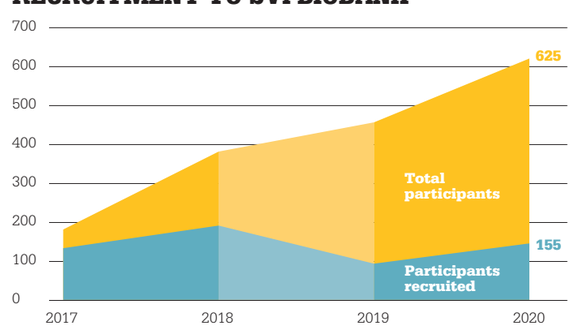
HIGHLIGHTS

We have been delighted to welcome Dr Katherine Woods as our Biobank Co-ordinator. Katherine brings a wealth of knowledge and significant experience to the repository and the safety and quality of sample processing and storage. The following projects commenced in 2020:

- BANDIT Phase 2 clinical trial is a Phase 2 randomised, placebo controlled study investigating the efficacy of Baricitinib in early onset Type 1 diabetes mellitus. The BANDIT clinical trial commenced in November and aims to recruit 83 early-onset type 1 diabetes patients, who will be monitored over the course of two years. Fourteen study visits will occur, and samples are taken for Biobanking on at least six occasions. Trial samples from three Melbourne hospitals will be processed by SVI Biobank - St Vincent's Hospital Melbourne, Royal Melbourne Hospital, and Royal Children's Hospital Melbourne. By the end of 2020, 16 participants were recruited, who have made a total of 26 visits, with 385 specimens stored for the trial.
- A breast and endocrine cancer clinical research project is one of our largest studies in collaboration with the St Vincent's Hospital surgical department. Researchers are collecting, and the biobank is storing, matched tumour and normal tissue and sequential blood samples from patients suffering from Breast and Endocrine cancers. The samples are being collected for use in a range of downstream research projects. Well annotated collections of this type are difficult to acquire and some samples have been sent to collaborating interstate laboratories and are critical for their research projects. In the first seven months, our collaboration with the surgical department has resulted in the recruitment of 102 participants for this study, with a total of 192 repeat visits and 2,064 blood and tissue specimens collected.

Accreditation... provides consumer confidence in our protocols and services by ensuring consistent service excellence in samples banked and stored.

ANNUAL AND OVERALL PARTICIPANT RECRUITMENT TO SVI BIOBANK



TESTING SERVICES

The critical task of ensuring accurate patient diagnosis is often left to highly specialised reference and confirmatory testing laboratories.

NRL is proud of its reputation as a screening & confirmatory laboratory for infectious disease testing

NRL is proud of its reputation as a screening and confirmatory laboratory for infectious disease testing, including services such as reference testing, screening of blood and tissue donors and contract testing.

Utilising validated testing strategies, NRL Testing operates as a reference laboratory for HIV, HCV and HTLV specimens whose status cannot be resolved by routine screening or other diagnostic laboratories. As a GMP-accredited laboratory, NRL performs TGA-licensed screening of blood and tissue donors for HIV, HBV, HCV, HTLV and Syphilis. Where IVDs are not validated for alternative sample types, NRL offers TGA-licenced testing of cadaveric samples for use in certain serology and molecular IVDs.

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

- Development of new assays
- Validation of testing algorithms
- Epidemiological studies
- Clinical trial support

The NRL Testing Team maintains an extensive repository of well characterised samples (Sample Bank) that is integral to its QA and Evaluation programs.

HIGHLIGHTS

- Provision of TGA-licensed screening of samples collected from living and cadaver blood and tissue donors, reference testing, and contract testing for projects
- Collaboration with the Alfred Hospital Pathology Service (APS) in early 2020 by making our Roche cobas 6800 System available and Testing Services playing a crucial role by supporting the training of APS laboratory staff while their new system was being installed and which was able to be commissioned ahead of schedule.
- Conducted a study investigating the potential risk of SARS-CoV-2 virus nucleic acid cross-contamination on Roche cobas 6800 system that used organ and tissue donor screening for HIV, HCV, and HBV.
- Participation in the ASHM Working Parties and contribution to the Review of the Australian National Testing Policies for each of Hepatitis B, Hepatitis C and HIV.

DATA

- 6498 Routine tests performed for donor screening and Reference Testing
- 5448 tests performed for EQAS Reference testing and sample characterization
- 952 HCV VL tests performed for the FIND Project
- 54 HTLV tests performed for HTLV NHMRC project
- 955 Proficiency tests performed

NRL Testing operates as a reference laboratory for HIV, HCV & HTLV specimens whose status cannot be resolved

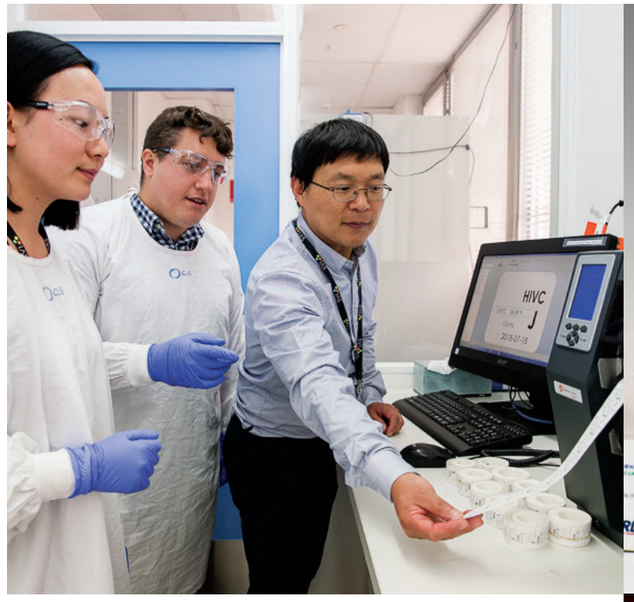
EQAS

External quality assessment schemes (EQAS) are vital in assessing the integrity of the entire infectious diseases testing process by identifying and resolving any potential sources of error, ultimately preventing the misdiagnosis of infection.

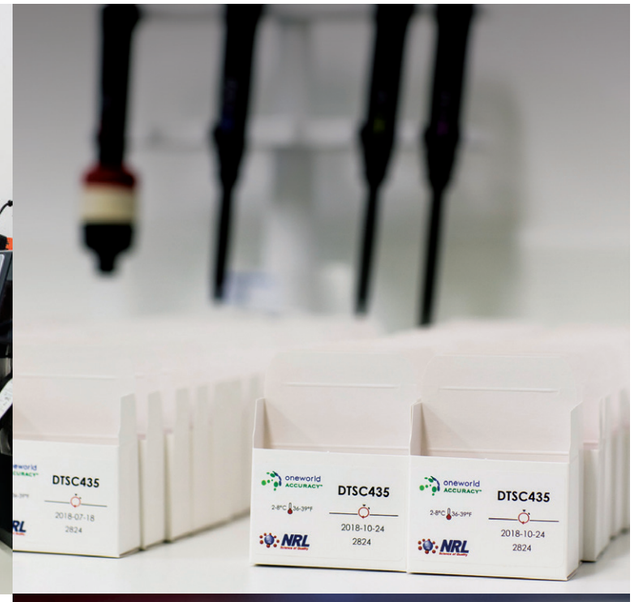
NRL is a global leader in the provision of external quality assurance programs, offering our services to over 50 countries and hundreds of pathology providers...

NRL is a global leader in the provision of external quality assurance programs, offering our services to over 50 countries and hundreds of pathology providers. As part of the comprehensive suite of quality assurance services that NRL provides, NRL EQAS incorporates scientifically designed panels comprised of positive and negative samples of known analyte. Assessment begins from sample receipt through to the final reporting and interpretation of the test result. In Australia, HIV, HCV and HTLV EQAS provided to diagnostic laboratories was supported by the Australian Government Department of Health until the end June 2020.

Panels are comprised of sample types that are representative of specimens normally received by a laboratory such as plasma, as well as alternatives such as dried tube samples (DTS) for use by those working in remote communities or low- and middle-income countries. NRL provides undiluted and diverse samples through material transfer agreements (MTAs) with collaborating blood transfusion services under which plasma packs screened as positive to infectious diseases and marked for discard, are provided for use in NRL's QA programs. NRL EQAS is accredited to ISO 17043 and includes specifically designed single and multi-analyte programs for Blood Screening, Clinical NAT, Clinical Serology and Point-of-Care (POC) testing.



NRL's EQA programs are provided in partnership with Oneworld Accuracy (1WA) Vancouver, Canada. EQAS participants submit testing results online via an internet-based application known as OASYS, developed by 1WA; used globally as a collection and analysis tool for external QA data aggregation and analysis. All results are assessed by NRL and reported in a final summary incorporating peer comparison and recommend-ations where required. Participants may verify the accuracy of their test result by comparing submitted results to the panel reference results. Each participant receives laboratory- and test-specific reports written by the NRL scientists.



IMPACT

In 2020, the EQAS Team embarked on a comprehensive review of the composition of the programs offered, with a view to making them more scientifically robust, improve reporting timeframes and better value for money.

Online informatics platform provider, Oneworld Accuracy is used globally as a collection and analysis tool for EQA data aggregation and analysis. During 2020, NRL staff worked with 1WA to propose and verify informatic system improvements including graphical data presentations, improved data entry and enabling reduced reporting timeframes. The EQAS provided by NRL are accredited to ISO17043. Some programs are multi-analyte; for example, blood screening serology and molecular testing; clinical nucleic acids for infectious disease such as *C. trachomatis and N. gonorrhoeae* and similarly for some serology and those for point of care programs.

HIGHLIGHTS

The achievements for the year and outcome of this review resulted in:

- A rejuvenated menu of programs and the introduction of several new multi-marker programs for release in 2021, which better reflect syndromic combinations experienced in laboratory testing.
- Preparation for a SARS-CoV-2 molecular program to be introduced to the Respiratory program
- Successful delivery of panel samples to almost the entire customer base in over 40 countries, despite the significant challenges and interruptions to freight and supply lines due to the global pandemic.
- Assurance of business continuity throughout pandemic lockdowns and uncertainty with panel production completed on time and in full during a COVID19 affected year

DATA

- 25 programs delivered across 40 countries and hundreds of sites

NRL EQAS incorporates scientifically designed panels comprised of positive & neg-ative samples of known analyte.

SCIENTIFIC EDUCATION, TRAINING & CONSULTING

High-quality testing is vital to ensure that appropriate diagnosis, treatment and ongoing management is provided to patients.

As a WHO Collaborating Centre for Diagnostics & Laboratory Support for HIV/AIDS and other blood-borne infections, NRL staff are highly regarded as consultants and technical expert

NRL's training and consulting services are culturally sensitive and customised to locally identified needs and we partner and collaborate to ensure that our capacity building activities are sustainable and effective. As a WHO Collaborating Centre for Diagnostics & Laboratory Support for HIV/AIDS and other blood borne infections, NRL staff 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.

IMPACT OF THE COVID19 PANDEMIC

NRL hosts workshops in both Australia and Asia annually as education fora for medical laboratory scientists, regulators, IVD manufacturers and clinicians working in the field of infectious diseases. The workshops are focused on laboratory quality, regulatory issues and infectious disease testing and facilitate the exchange of information, knowledge, experience and diverse perspectives among those working in communicable diseases nationally and internationally.

We were disappointed that our 2020 Asian Workshop in Manila from March 3-4 2020 and the WHO side meeting for the Regional Laboratory Network for Hepatitis Testing, being hosted by NRL, needed to be cancelled due to the risks of the evolving pandemic. The Australian Infectious Diseases Symposium in Melbourne in October was also cancelled. However, our focus was turned to virtual education, support and capacity building from Melbourne. No doubt one of the ongoing and significant benefits evolving from COVID19 is the effective and global ability for us all to now meet virtually — with time zones as the only barrier!

HIGHLIGHTS

- Collaborating with The Mérieux Foundation and Integrated Quality Laboratory Services (IQLS), the South-east Asia Laboratory Strengthening (SEALAB) project was commissioned to reinforce national health systems in Cambodia, Laos and Myanmar 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. Funded by the Indo-Pacific Centre for Health Security at the Australian Department of Foreign Affairs and Trade, under the ASEAN-Pacific Infectious Disease Detection and Response (APIDDaR) program, NRL's role was to assess capacity and deliver systems and training to strengthen the quality of testing performed in human laboratories. Due to the pandemic, much of the work was delivered virtually from Australia by working closely with other project staff in-country.
- The COVID19 pandemic realised much greater opportunity and acceptance for the virtual delivery of training programs and mentorship. Under a project funded by the US. President's Emergency Plan for AIDS Relief (PEPFAR), through a cooperative agreement between ICAP at Columbia University and the US Centers for Disease Control and Prevention (CDC) a training module on HIV Confirmatory testing was provided remotely to 90 laboratory participants in Myanmar in July, rather than face to face.. The effectiveness of training was demonstrated through improvement in pre-and post-training questionnaires, and further training was delivered including on the Stepwise Process to Improve the quality of HIV Rapid Testing (SPI-RT) and the verification protocol for the roll-out of HIV self-testing in Myanmar. NRL also supported the development of a validation protocol for reference HIV testing algorithm, a national certification framework for HIV testers and testing sites in Myanmar, and guidance documents on HIV self-testing.
- NRL staff delivered WHO guidance for end-users on how to conduct quality monitoring of in-vitro diagnostics (IVDs) and to develop use cases for better supply of end-user quality control materials and proficiency testing panels that are suited to testing in remote and regional locations which are physically difficult to access. In association with the WHO Regulation and Safety (REG)/ Incidents and Substandard/Falsified Medical Products (ISF) group, NRL developed these guidelines to inform Global Fund and other procurers of near-patient testing IVDs on how to establish a quality assurance and post-market framework. The IVD Quality Framework was focused on the needs of low resource settings where rapid diagnostic tests (RDTs) are generally used for diagnosis being per-formed by lay providers, community health workers and other non-laboratory trained healthcare workers.
- A new partnership was formed between NRL and Yayasan KNCV Indonesia (YKI) in 2020, with NRL conducting virtual EQAS training for the Republic of Indonesia Ministry of Health's four Provincial Health Laboratories, Balai Besar Laboratorium Kesehatan (BBLK) Jakarta, Palembang, Makassar and Surabaya. The training was facilitated by YKI, funded by the Global Fund for AIDS, Tuberculosis and Malaria (GFATM) and supported by the National AIDS Program at the Ministry of Health in Indonesia, and aimed to strengthen the quality of current EQA programs as well as enable the BBLKs to provide HIV viral load and early infant diagnosis EQAS by 2022.

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RESEARCH & DEVELOPMENT

NRL is a facility that enables new ideas and products to be brought to market.

While our specialist and historic background is in blood-borne infectious disease diagnostic testing, our skills and expertise can be applied to other infections and indeed outside infectious diseases.

Such capability is not common in academia because it does not involve breakthrough or discovery research but is an essential aspect of increasing the "D" in R & D. Given NRL's close association with and expertise in regulatory affairs of IVDs; our assay development capabilities and our assay evaluation capacity; we are well situated to expedite the translation of research into commercially ready products and services.

While our specialist and historic background is in blood-borne infectious disease diagnostic testing, our skills and expertise can be applied to other infections and indeed outside infectious diseases. We have mature skills in regulatory affairs from many years of working with the TGA, well-developed quality systems; expert knowledge in diagnostics and laboratory medicine; and in the provision of regulatory support. Our partnerships and collaborations with QC and device manufacturers and other commercial/ pharma partners extend globally & strengthens the relationships and expertise we bring to the table.

IMPACT

Following the appointment of Prof Rosemary Ffrench as Executive Manager, Clinical and Research Services in 2019, our dedicated R&D Team was established and greatly strengthened in 2020. Our collaborators included the Burnet and Doherty Institutes, as well as the National Measurement Institute, Rose represented NRL as a member of the Australian COVID-19 Sero-surveillance Network, the Scientific Advisory Committee of the COVID Victorian Diagnostics Consortium and is also a member of the TGA Advisory Committee on Vaccines (ACV).

Our support for indigenous health and HTLV1 continued through participation and support for the HTLV1 Working Party of the Australasian Society for HIV, Hepatitis and Sexual Health Medicine where clinicians and researchers work to raise awareness and guide clinical, public health and community response to infection.

Under the leadership of Wayne Dimech and funded by Global Fund, NRL was contracted by the WHO to deliver an IVD Quality Framework Document detailing novel approaches for quality control materials and proficiency testing panels for point of care (POC) testing in non-laboratory settings; meeting the needs of lower-middle-income countries, where rapid diagnostic tests (RDTs) are commonly performed by lay providers, community health workers and other non-laboratory trained staff.

NRL was contracted by the WHO to deliver an IVD Quality Framework Document detailing novel approaches for quality control materials and proficiency testing panels for point of care (POC) testing in non-laboratory settings

HIGHLIGHTS

- Collaboration with Burnet Institute and Doherty Institute on a Victorian Government initiative to develop novel Serology tests for COVID19 to monitor the development and waning of antibody responses to SARS-CoV-2. Our collaborators at the Burnet developed an immun-oassay and rapid point of care test (POCT) for the development of dimeric IgA in patient serum post infection. NRL established a western blot assay to assess the development of antibody responses of different isotypes over time, including IgM, IgG and IgA and sub-classes & differentiate the proteins to which the person is responding.
- Establishment of a repository of serum, plasma and Peripheral Blood Mononuclear Cells from SARS-CoV-2 infected donors which included cross sectional and seroconversion panels. In addition, a very large COVID19 plasma bank of well characterised samples was established with the support of our QC manufacturing partners Technopath Clinical Diagnostics and DiaMex GmbH. This resource then enabled our EQAS and Evaluations program.
- Collaboration with the National Measurement Institute (NMI), the Australian Government national authority on measurement, to create an Australian standard for SARS-CoV-2 RNA. Using inactivated virus obtained from Doherty Institute under Material Transfer Agreement, NMI created dilution series that was verified by all collaborators. The project created both a national standard as well as additional reference standards used to calibrate and validate molecular assays.
- Continuation of our work in Indigenous health in a collaborative project with the Burnet, Doherty and Baker Institutes, aimed at repurposing and validating the use of a POC sample collection device (the VL-Plasma® device) for use in HTLV-1 proviral load and antibody testing. This work is hoped to greatly aid the diagnosis and clinical management of HTLV-1 and associated conditions in indigenous Australians living in remote communities in Central Australia and was funded by the Australian Centre for HIV and Hepatitis Virology Research (ACH2).

EVALUATIONS

The analytical performance of a test kit otherwise known as an in-vitro diagnostic device (IVD) is an essential part of an effective testing strategy to ensure high-quality results to enable accurate diagnosis of infection.

NRL specialises in assessing the analytical and clinical performance of IVDs that detect infectious diseases to ensure they meet their stated intended use and conform to key performance, quality and safety criteria.

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 fourteen 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 conducts laboratory assessments of IVD performance on behalf of the WHO Prequalification of Diagnostics Program, the Therapeutic Goods Administration (TGA), Foundation for Innovative New Diagnostics (FIND) and commercial IVD manufacturers.

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

IMPACT

NRL undertakes post market review of SARS-CoV-2 (COVID-19) serology based point of care tests on behalf of the TGA and Doherty Institute.

SARS-CoV-2 is a beta coronavirus that causes COVID-19 which has been shown to be transmissible through various pathways. Individuals may exhibit signs and symptoms of acute respiratory illness, such as fever, cough, shortness of breath, but can also be asymptomatic. SARS-CoV-2 was the cause of the global pandemic that originated in late 2019.

Following the initial laboratory detection of the virus and release of the viral whole genome sequence by Chinese investigators in early January 2020, there was a rapid development of serological assays for SARS-CoV-2.

The urgent need for diagnostic testing resulted in many test kits undergoing expedited assessment from the TGA and allowed for emergency use. Due to this, post-market validation of SARS-CoV-2 diagnostic kits listed on the Australian Register of Therapeutic Goods (ARTG) was subsequently undertaken. The TGA aimed to review approved serology-based SARS-CoV-2 point-of-care tests (POCTs) to verify their ability to detect antibodies to SARS-COV-2 taking into consideration the timeframes for an individual to develop detectable levels of antibody.

Contracted by the Doherty Institute, fourteen of these assessments were undertaken by NRL Evaluations. These rapid diagnostic tests were assessed using a panel of well-characterised samples to allow comparison of performance across test kits. Data analysis for each assay was compiled and Summary Reports posted on the TGA website. For many of the RDTS evaluated, the manufacturer claims of sensitivity (how well the test can detect true positive SARS-CoV-2 infections) and specificity (how well the assay can detect true negative SARS-CoV-2 infection) were over-estimated. This may be due to the small set of panels analysed or other factors.

Knowing this information and the impact the SARS-CoV-2 pandemic has had on population health and the economy globally, it is paramount that IVDs utilised for detection of infectious diseases are of high quality and meet their stated claims. NRL's service in evaluating IVDs to ensure they are fit for purpose in accurately detecting infectious disease pathogens has never been more essential and significant.

HIGHLIGHTS

- Two Laboratory Performance Evaluations of HCV Molecular Assays for WHO Prequalification
- A Laboratory Performance Evaluation of a HCV Rapid Test for WHO Prequalification
- A Laboratory Performance Evaluation of a Syphilis Rapid Test for WHO Prequalification
- Fourteen SARS-CoV-2 antibody rapid diagnostic test (RDT) post market assessments on behalf of the TGA and the Doherty Institute
- Support for WHO in the development of protocols for assessment of anti-SARS-CoV-2 tests for emergency use

DATA

- 4 - WHO Prequalification Laboratory Performance evaluations
- 14 - Post-market IVD assessments on behalf of the TGA
- 6 - Customised panel sets consisting of a range of analytes for ToRCH, STI and anti-SARS-CoV-2 testing

NRL'S CONTRIBUTION TOWARD THE WHO PREQUALIFICATION OF IN-VITRO DIAGNOSTICS FOR HCV

Found world-wide, the hepatitis C virus (HCV) can cause ongoing inflammation of the liver leading to liver cirrhosis and cancer in individuals, as well as viral hepatitis-related deaths. It is estimated that 71 million people worldwide have chronic hepatitis C virus infection.

A WHO study found that an estimated 4.5 million premature deaths could be prevented in low- and middle-income countries by 2030 through vaccination, diagnostic tests, medicines and education campaigns1. In May 2016, The World Health Assembly adopted the first "Global Health Sector Strategy on Viral Hepatitis, 2016-2021"5. The strategy aims to eliminate viral hepatitis as a public health problem by reducing new viral hepatitis infections by 90% and reduce deaths due to viral hepatitis by 65% by 2030[5]. A component of this strategy includes scaling up screening of the population for HCV.

During 2020, as a WHO Collaborating Centre for Diagnostics and Laboratory Support for HIV and AIDS and Other Blood-borne Infections, the NRL Evaluations team undertook a number of Laboratory Performance Evaluations for HCV molecular and HCV serology IVDs for WHO Prequalification.

It is this work that helps establish accessibility to quality-assured, safe and effective IVDs for use in under-resourced regions in helping to address the burden of HCV globally. Access to therapeutics has increased the importance of the accuracy of testing and appropriately identifying those who will truly benefit from these treatments.

NRL's service in evaluating IVDs to ensure they are fit for purpose in accurately detecting infectious disease pathogens has never been more essential and significant.

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Dimech W, Westgard S
The SelectScience Virtual Science Summit

Quality Assurance of Infectious Disease Testing
Wayne Dimech
Sponsored by Sysmex Asia Pacific
For Philippines Laboratories
September 2020

IAEA and WHO-WPRO Webinar Series to support the COVID-19 testing laboratories in the Asia and the Pacific Region
Wayne Dimech
WHO WPRO and International Atomic Energy Association
30 September 2020

GLOBAL REACH

STAKEHOLDERS

- Abacus dx
- Abbott
- Alice Springs Hospital
- AusDiagnostics
- Australian Centre for HIV and Hepatitis Virology Research (ACH2)
- Australian Global Health Alliance
- Australian Government Department of Health
- Australian Red Cross Lifeblood
- Australasian Society for HIV, Hepatitis & Sexual Health Medicine
- Balai Besar Laboratorium Kesehatan Jakarta
- Balai Besar Laboratorium Kesehatan Palembang
- Balai Besar Laboratorium Kesehatan Makassar
- Balai Besar Laboratorium Kesehatan Surabaya
- BD Life Sciences Blood and Tissue Donation Services
- Becton Dickinson
- Bio-Rad Laboratories Pty Ltd
- Burnet Institute
- Central Public Health Laboratory, Papua New Guinea
- Cepheid China
- International Transfusion Infection Control
- CSL Behring Australia
- Department of Health and Human Services, Victoria
- Department of Health, Hong Kong
- Department of Health, Papua New Guinea
- DiaMex GmbH and Technopath Clinical Diagnostics, Tipperary, Ireland
- DiaSorin Australia Pty Ltd
- DKSH
- Exact Diagnostics
- Flinders University International Centre for Point-of-Care Testing
- Foundation for Innovative New Diagnostics
- Genetic Signatures
- Hologic
- ICAP at Colombia University, Myanmar
- Indo-Pacific Centre for Health Security
- Integrated Quality Laboratory Services (IQLS)
- Infectious diseases testing laboratories
- Institutions providing samples for NRL programs
- International Leptospirosis Society
- International Plasma and Fractionation Association
- Irish Blood Transfusion Service
- IVD Manufacturers
- Kirby Institute
- Logical Freight Solutions
- Ministry of Health and Sports, Myanmar
- MP Biomedicals Australasia Pty Ltd
- National AIDS Program, Myanmar
- National AIDS Program, Ministry of Health, Indonesia
- National Association of Testing Authorities, Australia
- National Health Laboratory, Myanmar
- New South Wales Ministry of Health
- New Zealand Blood Service
- Oneworld Accuracy, Canada
- Other selected QA program providers
- Pathology Technology Australia
- Peter Doherty Institute for Infection and Immunity
- PRONTO!
- QIAGEN
- Roche Diagnostics Australia
- Shanghai Blood Centre Siemens Healthineers
- South African National Blood Service
- SpeeDx
- St Vincent's Hospital Melbourne
- St Vincent's Hospital Sydney
- Sysmex, Japan
- Technopath Clinical Diagnostics
- The Mérieux Foundation (FM)
- Therapeutic Goods Administration
- United States President's Emergency Plan for AIDS Relief
- US Centres for Disease Control and Prevention
- Victorian Infectious Diseases Reference Laboratory
- World Health Organization Headquarters and Regional Offices
- World Health Organization Member States
- Yayasan KNCV Indonesia

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