NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

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Intern Scientist Training Programme – Molecular Biology

National Institute for Communicable Diseases

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1. Introduction

1.1 Background to the National Institute for Communicable Diseases

The National Institute for Communicable Diseases (NICD) provides laboratory based surveillance and diagnostic testing for diseases of public health importance to South Africa and the Southern African region. The NICD also sends outbreak response teams to sites confronted with infectious disease epidemics. The NICD houses national and regional referral laboratories. The NICD comprises ten centers, each of which focuses on different diseases, including HIV, Tuberculosis, malaria, diarrhoeal diseases and meningitis. The NICD serves as an expert authority, providing advice to Department of Health and medical practitioners. The NICD is a resource to all universities and technical colleges in South Africa, with multiple training programs in place and a strong complement of university-affiliated staff. The NICD is a division within the National Health Laboratory Service (NHLS), the national laboratory diagnostic network.

The Molecular Biology aspect of training encapsulates teaching and training across various centres within the NICD: Centre for Vaccines and Immunology (CVI), Centre for Enteric Diseases (CED), Centre for Emerging Zoonotic and Parasitic Diseases (CEZPD), Centre for HIV and STI (CHIVSTI), Centre for Respiratory Diseases and Meningitis (CRDM), Centre for Tuberculosis (CTB), Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses (CHARM).

At orientation:

(1) An overall explanation of the program will be provided to the intern
(2) Expectation of the program will be discussed as per training program
(3) Training dates
(4) Discuss- logbook, self-assessment, written tests/exams, evaluations, affiliations to professional societies
(5) An interim program will be discussed (an in-depth training program and timelines will be discussed in more detail for the respective laboratories)
(6) An evaluation report to be completed after rotation in each laboratory (Appendix 1).
(7) A list of supervisors and contact details is provided (Appendix 2)

1.2 Optional Host Centres with specific competencies

1.2.1	Centre for Vaccines and Immunology
1.2.2	Centre for HIV and STI

1,2.3	Centre for Respiratory Disease and Meningitis
1.2.4	Centre for Enteric Diseases
1.2.5	Centre for Tuberculosis
1.2.6	Centre for Opportunistic, Tropical and Hospital Infections
1.2.7	Centre for Emerging and Zoonotic Diseases
1.2.8	Sequencing Core Facility

1.2.1 Centre for Vaccines and Immunology

The Centre for Vaccines and Immunology provides laboratory support to South African and Southern African departments of health for surveillance of vaccine preventable diseases including acute flaccid paralysis (polio), measles, rubella, hepatitis A, hepatitis B, hepatitis C, enterovirus and tetanus. Specialized molecular diagnostic services are offered.

Polio testing

In support of the Global Poliomyelitis Eradication Initiative (GPEI) initiated in 1988 by the World Health Assembly, any new onset of hypotonic weakness (acute flaccid paralysis) in a child aged less than 15 years of age is investigated for poliovirus. Acute flaccid paralysis surveillance is a GPEI strategy to detect poliovirus circulation, re-importation of wild poliovirus into polio free-areas or regions and emerging vaccine derived polioviruses (VDPVs).

The Centre for Vaccines and Immunology is a national and World Health Organization accredited regional referral laboratory for AFP surveillance. The Centre conducts poliovirus isolation and identification for South Africa, Angola, Botswana, Lesotho, Mozambique, Namibia, Swaziland, Angola and the Democratic Republic of Congo. The Centre also conducts environmental surveillance for South Africa, Angola, Mozambique, and Zambia. Molecular analysis is performed by sequencing for PCR discordant samples and Poliovirus 2. Testing involves three aspects – maintenance of sterile cell lines, isolation of stool samples into cell lines with daily monitoring for cytopathic effects, and molecular typing of strains using polymerase chain reaction (PCR) and sequencing. Reporting of isolates and sequence information is performed weekly according to standardized templates in the format required by the World Health Organization. Results are also given to clinicians treating the patients.

Polio immunity testing is conducted using a microneutralisation assay. This is a labor-intensive assay used to measure functional antibodies, which block polio entry into cells. We are one of the few laboratories in the country still performing viral neutralization assays, allowing intern scientists a rare opportunity to become familiar with the methodology.

Measles testing

As one of the most contagious infectious disease, measles virus causes significant morbidity and mortality in children, and especially those who are malnourished and/or immune-compromised. Since the aim of Millennium Development Goal 4 is to reduce the overall number of deaths among children under 5 years of age by two-thirds from 1990 to 2015, routine measles vaccination coverage was selected as an indicator of progress towards this goal. Aggressive efforts to improve measles vaccination coverage resulted in an estimated 86% reduction in measles-related mortality globally between 1990-2008, representing a 23% reduction in all-cause mortality in the under-5 age group in this period.

The Centre for Vaccines and Immunology is the national and WHO regional referral laboratory for measles surveillance. Serology, specifically the detection of measles-specific IgM antibodies, is the most commonly used method of laboratory diagnosis of acute measles infection. The Centre provides a diagnostic service to referring clinicians. Additionally the Centre provides reference testing for the external quality assurance program run by the World Health Organization for measles. The Centre also uses PCR and sequencing to genotype measles strains and analyze the phylogenetic trees for any measles outbreak. Molecular

epidemiology provides information to authorities regarding geographic distribution and evolution of measles strains.

Rubella
Rubella surveillance is performed by serology using febrile rash surveillance samples. Since rubella presents with similar clinical symptoms to measles, laboratories often test for IgM against both viruses in suspected measles cases. IgM is a marker of recent infection. Avidity assays may be useful in certain cases. There is also surveillance for congenital rubella syndrome through the notifiable medical conditions system and active sentinel site surveillance.

Hepatitis B testing
Hepatitis B vaccination was introduced into the South African Expanded Programme of Immunization in 1995. The HIV epidemic has increased the burden of disease in South Africa from Hepatitis B. The Centre for Vaccines and Immunology provides laboratory-based surveillance for hepatitis B performing data mining from the NHLS corporate data warehouse and periodic sero-surveys on residual sera from other surveillance programs. The Centre is involved in hepatitis B projects, often including genotyping to identify circulating strains of hepatitis B. Genotyping gives a snapshot of the burden of disease caused by each strain.

Hepatitis C testing
There is currently no vaccine against hepatitis C and no national surveillance program. The burden of disease of hepatitis C in South Africa is not well defined. The Centre for Vaccines and Immunology provides laboratory-based surveillance in the form of data mining to inform on hepatitis C burden. Projects also use genotyping to identify the strain, which can provide prognostic information to the clinician.

Immuno-regulation laboratory
The immuno-regulation laboratory in the Centre aims to identify correlates of protection to Tuberculosis and other infectious diseases by characterizing the immune response and factors that limit the effectiveness of the immune response. Factors such as regulatory T cells, cytokines, Human leucocyte antigens and antibodies to Human leucocyte antigens are studied by flow cytometry and molecular methodologies.

Specialized Facilities and equipment in Centre for Vaccines and Immunology
- Thermal Cycler
- 7500 Real Time PCR System
- Horizontal Gel Electrophoresis Apparatus
- Flash Gel Dock
- UV Transilluminator
- Nanodrop Spectrophotometer
- Life Technologies 3500XL Genetic Analyser

Specific competencies from Centre for Vaccines and Immunology
- Neutralization assay for assessment of polio immunity
- Exposure to Intratypic differentiation (ITD) and Vaccine Derived Poliovirus (VDPV) screening of the Poliovirus using Real Time PCR
- Sequencing and analysis of the Poliovirus
- PCR for measles measles and or rubella viruses
- Genotyping measles and or rubella viruses
- Luminex based HLA typing

1.2.2 Centre for HIV and Sexually Transmitted Infections

The Centre for HIV & Sexually Transmitted Infections (STI) is a resource of knowledge and expertise in HIV and other regionally relevant STIs to the South African Government, to SADC countries and to the African continent at large, in order to assist with the planning of policies and programmes related to the control and effective management of HIV/STIs. The Centre also aims to be a place of academic excellence in terms of

both research and teaching/training. The Centre has a strong record of accomplishment in the research disciplines of HIV virology, HIV immunology, HIV/STI epidemiology, HIV/STI diagnostics and HIV-STI interactions, as well as in successful supervision of PhD and MSc students.

HIV prevalence and incidence surveillance

The Centre supports the National Department of Health's (NDoH) Annual Antenatal HIV-1 Prevalence and HIV Incidence survey and the South African Prevention of Mother to Child Transmission (PMTCT) Effectiveness study at 4-8 weeks post-partum. The latter survey is critical to inform on the continued success or otherwise of the decline in HIV transmission in the PMTCT setting. To improve surveillance of HIV incidence, methods are being applied to various surveys and since this methodology is new to the field in South Africa, optimum methods for analysis are being assessed.

HIV drug resistance surveillance

The Centre's HIV drug resistance laboratory is the designated Centre for national surveillance activities and also serves as a WHO regional HIV drug resistance laboratory. The laboratory has recently extended the scope of testing to include genotyping of dried blood spot specimens in addition to plasma, allowing for surveillance of resistance in pediatric patients. On-going surveys of transmitted resistance make use of specimens collected from young women in their first pregnancy who participate in the annual antenatal clinic survey. The laboratory also offers training to visiting scientists from local and sub-Saharan Africa.

STI clinical syndrome, aetiological and gonococcal antimicrobial resistance surveillance

The Gauteng STI surveillance project, run by the Centre in collaboration with the Gauteng Provincial Department of Health (DoH), collects STI syndrome data from public clinics. In collaboration with the NDoH, provincial DoHs, Alexandra Health Centre and NHLS laboratories, the Centre undertakes aetiological surveillance of three major STI syndromes (male urethritis syndrome, MUS; vaginal discharge syndrome, VDS; genital ulceration syndrome, GUS), as well as surveillance of gonococcal antimicrobial resistance, in Gauteng (Johannesburg), Mpumalanga (Nelspruit) and the Northern Cape (Kimberley) provinces. Molecular, serological and bacteriological methods are employed to test for a variety of STI pathogens

HIV-1 rapid testing quality assurance and post-marketing surveillance of HIV rapid test devices

The NDoH has expanded HIV testing in South Africa in the past three years with well over 15 million individuals tested. A critical component is the quality assurance of testing. PEPFAR-funded quality assurance coordinators conducted 235 on-site monitoring and evaluation visits to assess progress with HIV rapid testing and specifically the introduction of the use of internal quality assurance specimens as part of quality assurance monitoring. Three HIV rapid test kits were awarded the government tender in 2011. A key follow-on activity undertaken by the Centre was the post-marketing surveillance of the lots/batches of devices prior to release in testing sites.

HIV external quality assurance schemes

Centre staff coordinate the HIV EQA program for NHLS-participating laboratories. Serology panels are distributed to 181 laboratories and HIV RNA panels to 18 participating laboratories. Participation in the schemes is mandatory and reporting of both the serology and molecular scheme results as part of the quality improvement processes.

Support for HIV vaccine trials

The Centre provides results from validated end-point humoral antibody and molecular HIV assays for the HIV Vaccine Trial Network (HVTN).

Correlates of Protection against HIV-1

The Centre is involved with multiple projects to characterize innate and adaptive aspects of protection against HIV disease. These include the role of CCR5 and its ligands, the role of natural killer cells and the role of host genetics, particularly at the human leucocyte antigen (HLA) loci.

Equipment for Centre for HIV and STI

Areas for molecular work include the following: a nucleic acid extraction laboratory (18 m^2) with a MagNa Pure Extraction System, or NUcliSens easyMAG 2; the pre-PCR area (2 x 10m^2) with a UV light to decontaminate surface areas; and a post-PCR laboratory (80 m^2) with 10 PCR thermocyclers, a Gel-doc system, a Nanodrop spectrophotometer, a transiluminater, 2 Biocap extraction hoods and 3 electrophoresis power units. A separate laboratory (24 m^2) is available for bacterial work and contains a Biohazard class II safety cabinet. The sequencing laboratory (10 m^2) contains two Genetic Analyzers, a 3130xl and a 24 capillary 3500xl and 2 ultra-deep sequencing platforms, a 454 Junior and MiSeq. Currently these areas are utilized in the single genome amplification, sequencing and cloning of HIV-1 envelope genes.

Protein purification facilities include an AKTA Prime Pump, Chemi-doc gel system, SDS-PAGE tanks, Western-Blot equipment, a microplate washer and a microplate spectrophotometer.

Specific competencies from Centre for HIV and STI

HIV drug resistance genotyping

- Sample handling.
- Extraction of RNA from plasma and dried blood spots.
- PCR for HIV-1 *pol* gene.
- Sequencing of the PCR products.
- Sequence analysis using two softwares: Sequencher Version 5 and ReCall.
- Interpretation of HIV-1 drug resistance report from the Stanford database.

Bioinformatics for HIV drug resistance

- Align and edit sequences using Bioedit and Mega 5.
- Calculate genetic distances between patient viruses.
- Generate neighbour-joining tree and maximum-likelihood tree using Mega 5, PhyML and PAUP.
- Interpretation of phylogenetic trees and contamination identification.

1.2.3. Centre for Respiratory Diseases and Meningitis

Background

The Centre for Respiratory Diseases and Meningitis (CRDM) is a resource for surveillance, diagnostics, expertise and research in the field of communicable respiratory diseases and meningitis for South Africa and the African continent. The Centre generates data and provides expertise related to respiratory diseases and meningitis of public health importance to the South African national Department of Health, healthcare providers and regional and international collaborators, to assist with the planning of public health policies, programmes and response to respiratory disease and meningitis outbreaks. The Centre is also a source of capacity building and formal training within South Africa and the African region. CRDM includes bacteriology and virology laboratories, and a team of epidemiologists and surveillance field staff.

Specific competencies

- Molecular detection and serotyping/grouping of *S. pneumoniae*, *N. meningitidis* and *H. influenzae*
- Strain characterization of organisms using multi-locus sequence typing or whole genome sequencing
- Molecular detection of atypical pneumonia-causing pathogens (*B. pertussis, M. pneumoniae, C. pneumoniae, Legionella* spp.)
- Taqman Array Card technology for simultaneous detection of multiple respiratory pathogens (viruses and bacteria)
- Influenza and other respiratory virus isolation
    - Hemagglutination inhibition assays to determine sensitivity of circulating influenza viruses to vaccine-induced antibodies or to evaluate exposure to novel or zoonotic influenza a viruses and other respiratory pathogens and lastly this assay can be used to evaluate the immune responses induced in vaccine recipients.

- Conventional live virus based microneutralisation assays.
- Pseudovirion-based microneutralisation assays for BSL3 pathogens performed under BSL2 conditions
- Conventional PCR and sequencing of respiratory virus gene fragments
- Allelic discrimination real time RT-PCR assay to identify influenza B lineages and to identify known drug resistant mutation in the M and NA genes of influenza
- Phenotypic assay to determine sensitivity of influenza virus neuraminidases to antiviral drugs
- Multiplex real time RT-PCR for human respiratory viruses including influenza viruses
- Determination of cytokine levels in respiratory samples and/or other biological samples investigation of zoonotic respiratory viruses that cause respiratory / neurological symptoms
- Virus discovery for unknown causes of respiratory disease
- Genome sequencing using both Sanger and next generation sequencing methods

Specialized Facilities and equipment in Centre for Respiratory Diseases and Meningitis

- Thermal Cyclers
- 7500 Real Time PCR Systems and Roche 480
- ViiA7 real time PCR machine with block and centrifuge for TLDA cards
- Horizontal Gel Electrophoresis Apparatus
- Western blot apparatus with semi-dry transblot
- UV Transilluminator
- Nanodrop Spectrophotometer
- Bio-Rad Bio Plex 200
- Multi-label plate reader with stacker
- Glomax Luminometer
- GeneGnome imaging system for luminescence
- Bio-Rad Gel documentation system
- Magnapure 96 RNA extraction system
- Nanophotometer

1.2.4 Centre for Enteric Diseases

The Centre for Enteric Diseases (CED) is concerned with activities related to surveillance of pathogens associated with diarrhoea and enteric fevers, and investigation/response to enteric disease outbreaks (including foodborne and waterborne disease outbreaks). CED is tasked with developing strategies and providing information to combat diarrhoeal diseases in South Africa. CED monitors trends in diarrhoeal pathogen incidence and identifies areas for the introduction of additional interventions.

The bacterial division of the CED collects data on patients presenting throughout South Africa with both invasive and non-invasive disease caused by Salmonella species (including Salmonella Typhi), Shigella species, Vibrio cholerae, Listeria monocytogenes and diarrhoeagenic Escherichia coli. In order to make these data representative and reflective of disease burden in each province in the country, we actively motivate all diagnostic laboratories throughout the country to voluntarily submit limited demographic details and isolates to us centrally. In exchange, we offer serogrouping and serotyping results, regular feedback (quarterly reports by province sent to every laboratory participating) and aggregated numbers are published in the NICD Bulletin.

In addition to serogrouping and serotyping, E-tests are used to determine the minimum inhibitory concentration (MIC) of each isolate to antimicrobial agents, according to CLSI guidelines. The bacterial division also performs genotypic characterization of isolates, which includes various PCR tests and whole-genome sequencing (WGS) analysis. PCR tests are used to assist with diagnosis of particular pathogens and elucidate the presence of particular virulence (toxin) genes, such as those found in toxigenic E. coli and toxigenic V. cholerae. The molecular epidemiology of some bacterial pathogens is continually being elucidated, specifically that of outbreak or epidemic-prone pathogens such as Salmonella Typhi, L.

monocytogenes and V. cholerae O1. The molecular epidemiology of bacterial pathogens is investigated via WGS. Analysis of WGS data is used to assess the genetic relatedness of isolates, for investigation of clusters and outbreaks. Core-genome multi-locus sequence typing (cgMLST) and single nucleotide polymorphism (SNP) analysis, are the two most commonly used tools to assess the genetic relatedness of isolates. These WGS data are interpreted together with epidemiological data to assist with investigation of outbreaks and identification of the source of outbreaks.

The introduction of the rotavirus vaccine into the national expanded program of immunization (EPI) in August 2009 was a positive step in combating diarrhoeal disease burden in children < 5 years in South Africa. The viral division of the CED has been tasked with monitoring the impact of the rotavirus vaccine and surveillance is planned to continue into 2015. Projects investigating rotavirus vaccine safety, optimal vaccine use, and improved vaccine efficacy are also being undertaken and will generate practical regional data for African countries considering introducing the rotavirus vaccine.

While rotavirus cases are being reduced by the introduction of efficacious vaccines, the remaining 70% of diarrhoeal cases need to be investigated. Stools collected through the rotavirus sentinel surveillance program are examined via an integrated diagnostics platform within the divisions of the CED. Surveillance for enteric viruses, other than rotavirus, has previously only been conducted on an *ad hoc* basis and the contribution of mixed pathogen infections has never been studied in the South African population. Expansion of the current diarrhoeal surveillance program to include more sentinel sites and offer a wider range of screening options will increase the quality and representativeness of the data generated.

Specific competencies in Centre for Enteric Diseases

- *Salmonella* species: identification, serotyping and antimicrobial susceptibility testing
- *Shigella* species: identification, serotyping and antimicrobial susceptibility testing
- *V. cholerae* (O1 and non-O1): identification, serotyping and antimicrobial susceptibility testing
- Diarrhoeagenic *Escherichia coli*: identification (via conventional PCR to detect for virulence genes), serotyping and antimicrobial susceptibility testing
- *Listeria monocytogenes*: identification and antimicrobial susceptibility testing
- Stool processing to extract DNA and RNA
- *Campylobacter* species: real-time PCR identification
- *V. cholerae* and cholera toxin: real-time PCR identification
- *Salmonella* species, *Salmonella* Typhimurium and *Salmonella* Enteritidis: real-time PCR identification
- Whole-genome sequencing (WGS) of bacteria
- Analysis of WGS data to investigate the genetic relatedness of bacterial isolates
- Analysis of WGS data using multi-locus sequence typing (MLST), core-genome MLST and single nucleotide polymorphism analysis
- Rotavirus: detection and genotyping via ELISA and RT-PCR
- Adenovirus: detection via ELISA and real-time PCR
- Norovirus: detection via real-time PCR
- Astrovirus: detection via real-time PCR

1.2.5 Centre for Tuberculosis (CTB)

Functions of the CTB include provision of specialist diagnostic services, policy development and standardization of diagnostic methods, and the development and evaluation of novel technologies to advise strategic planning and policy. Further functions concern developing an integrated surveillance system; providing epidemiological data for the public, government and scientific community; and utilizing surveillance and microbiological data to design and implement research on a national basis. In addition to these, the Centre will continue to support the National Department of Health (NDoH) in the development of new TB guidelines and policy, support training programmes and work towards the detection, integration and response to outbreaks. The CTB provides support for the government of South Africa‘s objective for its 2012-

2016 strategic plan of halving the number of new TB infections and deaths from TB by 2016. The Centre also plans to assist with TB control activities of other Southern African Development Community Countries.

Trends in multidrug-resistant TB and emergence of extremely drug-resistant TB

In 2010, there was an estimated prevalence of ~650000 cases of multidrug-resistant TB (MDR-TB) globally; while in 2008, there were ~1500 MDR-TB-related deaths. The World Health Organization (WHO) calculates that only 16% of the estimated number of MDR-TB patients that needed treatment in 2010 received treatment directed against MDR-TB. As part of the Global Project on Anti-Tuberculosis Drug Resistance Surveillance of the WHO/International Union against Tuberculosis and Lung Disease (IUATLD), a countrywide drug resistance survey was conducted in South Africa during 2000-2001. The survey recorded MDR-TB rates in the provinces, which varied from 0.9% to 2.6 % in new cases and from 3.9% to 13.7 % in retreatment cases. A second national drug resistance survey, details of which feature in this report, will be conducted in South Africa during 2012-2013.

The National Health Laboratory Service (NHLS) of South Africa provides facilities for mycobacterial culture and drug susceptibility testing (DST) covering rifampicin and isoniazid for the diagnosis of MDR-TB as well kanamycin/amikacin and the fluoroquinolones ofloxacin/moxifloxacin for the detection of extremely drug-resistant TB (XDR-TB) on a regional basis throughout the country.

Based on information extracted from the CDW, the numbers of laboratory-confirmed MDR-TB patients in eight provinces (figures for KwaZulu-Natal were not available on CDW) were 5348 in 2007and 6198 in 2010. The proportion of MDR-TB cases compared with newly diagnosed culture-confirmed TB cases during this period was 5.0%. During the same period, the numbers of XDR-TB patients diagnosed per year in the eight provinces increased from 260 to 454, constituting on average 6.2% of the annually diagnosed MDR-TB cases.

Monitoring of the genetic basis of resistance to anti-TB drugs

Not only is surveillance of the extent of resistance to anti-TB drugs important but monitoring of the genetic basis for such resistance is also a priority for the development and upgrading of rapid molecular methods for resistance detection, as well as formulating strategies for prevention and containment, and serving as a basis for new drug development. South Africa with its high prevalence of TB and suboptimal performance of directly observed therapy, short course (DOTS) and DOTS Plus for management of known or suspected drug-resistant TB, coupled with good laboratory facilities and expertise, offers ideal circumstances for the study of emerging and ongoing drug resistance. Unsurprisingly, study of the problem of drug resistance is receiving a very high priority in the 5-year business plan of the CTB and features in a large proportion of the projects envisaged in the plan.

Epidemiological research and need for enhanced surveillance

The realization of the importance of epidemiological research in the field of TB has led directly to the expansion of the National Tuberculosis Reference Laboratory (NTBRL) to include as an equal partner a well-staffed Epidemiology division in the newly established CTB. A highly experienced epidemiologist from the Health Protection Agency in the UK was specifically seconded to South Africa for three years to promote and expand epidemiological expertise and activities in this country, heads the Epidemiology division.

Epidemiological research planned for the next five years will focus on public health surveillance including the large drug resistance survey designed to be representative of TB drug resistance in the country. Projects include optimizing surveillance of TB utilizing routinely collected data from the CDW, an enhanced surveillance project comprising sentinel surveillance of rifampicin-resistant TB and studying the emergence of rifampicin mono-resistance in the country, and surveillance of TB in hospitalized patients with severe respiratory illness, using an existing GERMS surveillance network in South Africa

<u>Specialized Facilities and equipment in Centre for Tuberculosis</u>

The Centre for Tuberculosis laboratory facilities include a P3 laboratory for handling of viable infectious agents and a P2 laboratory for downstream molecular and typing applications. Our Laboratories have a range of conventional and molecular diagnostics used for the detection of tuberculosis.

P3 Facility: 356m^2

The P3 facility is separated into three sections, which include dedicated Culture laboratory, Microscopy and Molecular Laboratory and Drug Susceptibility Facility.

P2 Facility: 331m^2

The Facility consists of four fully equipped molecular biology laboratories for sample preparation, extraction, Conventional and Real-time PCR assay generation, Post amplification analysis, Sequencing and Typing analysis and storage. The Facility is dedicated to providing diagnostic services, Sequencing and Strain typing for Mycobacteria.

Specialized equipment

- Nucleasens Easy Mag extraction system
- BSC Class II
- PCR workstation
- ABI 3130 sequencer
- StepOne Plus Real-time PCR instrument
- Convention PCR thermocyclers
- Riboprinter
- Gel-Doc system
- X-Ray developer
- BioTek plate reader
- Gel Eletrophoresis system
- NanoDrop (DNA quantification)
- Twincubators (Hain Lifescience PCR detection)
- GT Blot (Hain Lifesciences PCR detection)
- Qubit analyser
- MiSeq sequencer

Specific competencies

- Performing Xpert MTB/Rif assay and interpreting results
- Perform MTBDRplus/CM/SLT assays and interpret results
- Perform Spoligotyping an MIRU-VNTR typing and analyse results including phylogenetic analysis
- Performing sequence run with library preparation on the MiSeq and interpreting sequence data with data quality assessment

1.2.6 Centre for Healthcare-associated Infections, Antimicrobial Resistance and Mycoses

The NICD's Centre for Healthcare-associated Infections, Antimicrobial Resistance and Mycoses (CHARM) serves as a national hub of expertise in the fields of:

1. Healthcare-associated infections (HAIs)
2. Antimicrobial resistance (AMR)
3. Mycoses

Relevant to these three focus areas, the Centre conducts/ provides:

1. Surveillance
2. Outbreak investigations
3. Public health-focused research
4. Reference laboratory diagnostic services

5. Teaching and training

Strategic information from these activities is shared with the South African Department of Health and other major stakeholders.

Healthcare-associated infections (HAIs)

- HAIs are among the commonest complications of a hospital admission, are costly for the patient and overall healthcare system and may lead to patient deaths
- This is an important ***new focus area*** for the Centre
- Plans are afoot to pilot surveillance for HAIs at sentinel hospitals and detect outbreaks at facility level
- The Centre is now involved in developing practical South African guidelines for hospital-level activities related to HAIs and AMR

Antimicrobial resistance (AMR)

- AMR is associated with >700000 deaths every year, a number which could rise as high as 10 million in 2050
- AMR is a major focus area of the South African Department of Health and the NICD
- The Centre works on AMR in bacterial and fungal pathogens causing human infections in healthcare facilities and in the community, spanning the public- and private-health sectors
- The Centre was named a World Health Organization Coordinating Centre for AMR in 2017
- CHARM is also a National Coordinating Centre for the WHO Global Antimicrobial Resistance Surveillance System (GLASS)
- Senior members of the Centre represent NICD on the Ministerial Advisory Committee for AMR
- Laboratory-based surveillance is conducted for priority pathogens, including carbapenemase-resistant Enterobacteriaceae, the "ESKAPE" bacterial pathogens and *Candida auris.* The Centre is also responsible for compiling electronic surveillance data from public- and private-sector laboratories across the country. Surveillance data support development of standard treatment guidelines for certain infectious diseases. The Centre has two reference laboratories which provide support for outbreak and reference activities related to AMR

Mycoses

- Over the last 5 years, NICD led implementation of a national cryptococcal antigen screening and pre-emptive treatment intervention, nested within the South African HIV treatment programme. The Centre is now involved in evaluating the effectiveness of this intervention to reduce mortality through an NIH R01-funded grant.
- The Centre contributed to discovery of emerging HIV-associated fungal pathogens such as the newly-described thermally-dimorphic fungus, *Emergomyces africanus*
- The Centre's mycology reference laboratory has expertise in antimicrobial resistance (AMR) for fungal pathogens and conducts national surveillance for candidaemia
- The Centre is involved in global efforts to improve access to antifungal medicines and fungal diagnostics

National stock culture collection (NSCC)

- The NSCC was established in April 2004 and is now housed within CHARM
- The Culture Collection provides a quality-controlled and reliable source of reference bacterial, fungal and mycobacterial strains to NHLS laboratories
    - Laboratories, which are accredited to ISO15189 as diagnostic medical laboratories, are required to control all procedures and tests.

    - Antimicrobial susceptibility and identification tests on bacteria/ fungi require reference strains on which control tests are performed.
- Strains are also available for teaching, training and research purposes
- The services of the NSCC were re-launched in February 2014 with development of a streamlined online ordering system, accessible via the NHLS intranet homepage
    - This system requires laboratories to upload the relevant permits and registrations required by legislation and to select the strains they require
    - There is traceability of strains until the order is received and acknowledged in the laboratory

The Centre for Healthcare-associated Infections, Antimicrobial Resistance and Mycoses aims to prevent and control opportunistic, tropical and hospital infections in South Africa by providing:

- Strategic information obtained through surveillance and research to the Department of Health and other major stakeholders
- Technical support for public health programmes such as the malaria control programme and the cryptococcal screening programme
- Reference laboratory services in the fields of parasitology, mycology, entomology and bacteriology Laboratory support for outbreak response
- Training for clinical, laboratory and public health personnel to ensure optimal diagnosis and control of diseases

The Centre focuses its efforts on opportunistic infections, particularly those that are HIV-related; tropical infections, especially malaria and its vectors; and nosocomial infections, concentrating on antimicrobial resistance in the hospital setting.

<u>Specialized Facilities and equipment in the Centre for Healthcare-associated Infections, Antimicrobial Resistance and Mycoses</u>

- Thermal Cycler
- Horizontal Gel Electrophoresis Apparatus
- G-Box Gel Documentation System
- UV Transilluminator
- Nanodrop Spectrophotometer

<u>Specific competencies from Centre for Opportunistic, Tropical and Hospital infection</u>

- Sequencing and Phylogenetic analysis of unknown / difficult fungi
- *Candida* species antifungal resistance genotyping (D- glucan synthase)
- Genotyping of *Candida parapsilosis*
- Genotyping of *Cryptococcus neoformans*

1.2.7 Centre for Emerging Zoonotic and Parasitic Diseases

The CEZPD aims to establish itself as a national and international Centre of excellence for emerging and parasitic diseases. CEZPD aim to function as a resource for knowledge and expertise to the South African government, the SADC countries and the African continent, in order to assist in the planning of relevant policies and programmes and to harness innovation in science and technology to support surveillance, detection and outbreak response systems. In observing this goal, the CEZPD supports South Africa's commitment to the International Health Regulations.

<u>Specialized facilities and equipment in the Centre for Emerging Parasitic and Zoonotic Diseases</u>

The CEZPD operates multiple biosafety level 3 laboratories and the only biosafety level 4 laboratory in South Africa. These facilities are geared for bacteriological, virological and animal work. In addition, the Centre operates several biosafety level 2 laboratories including PCR facilities and general molecular laboratories.

- Equipment for molecular biology applications includes:

- Lightcycler® v1.5 real time PCR machine (Roche)
- Lightcycler ® 480 real time PCR machine (Roche)
- Smartcycler II real time PCR machine (Cepheid)
- GeneAmp 2720 automated thermocyclers (Applied Biosystems)
- Real time turbimeter for loop mediated isothermal amplification (LAMP) (Teramecs)
- Agarose gel electrophoreses equipment
- Ultraviolet transilluminator with gel documentation system
- PAGE gel electrophoresis equipment
- Western blot equipment (i.e. semi dry and wet blotting equipment)
- Incubators, water baths, centrifuges, laminar flow cabinets, biosafety cabinets etc.

Specific competencies for Centre for Emerging Parasitic and Zoonotic Diseases

Performing and analysing molecular detection protocols for diagnosis of viral haemorrhagic fevers, rabies and arboviral infection including the use of real time, conventional and isothermal amplification protocols

Additional competencies:

- Molecular sequencing of PCR products and basic analysis of sequence data
- Basic molecular cloning techniques (PCR product clean up, TA or other cloning vector cloning, blue/white and antibiotic selection techniques)
- Basic protein expression techniques in bacterial, baculo- and mammalian expression systems

Parasitology Working Group

The group provides a specialized parasitology reference service for routine diagnostic medical laboratories. In addition, some important opportunistic pathogens form the focus of its diagnostic, research, teaching, and surveillance activities. *Pneumocystis jirovecii* is an unconventional opportunistic pathogen that causes the important AIDS-defining infection, Pneumocystis pneumonia (PcP). The estimation of the burden of PCP in HIV-positive patients at sentinel sites in South Africa is a current project. Other opportunistic diseases being studied are microsporidiosis, toxoplasmosis, and free-living amoeba infections. Malaria and echinococcosis are other areas of interest for the group.

Specific competencies for Parasitology

- PCR for *P. jirovecii*
- RFLP/ Sequencing for *P. jirovecii* DHPS genotypes
- Multiplex PCR for malaria
- PCR for microsporidia

1.2.8 Sequencing Core Facility

The Sequencing Core Facility aims to provide accurate, high quality and cost-effective next generation sequencing (NGS) solutions. The facility currently supports all centres at the NICD in terms of NGS and bioinformatic needs, thus it acts as an extension of every centre with regards to NGS capacity. Since its inception, the core facility has continually engaged in several projects from design to completion. Some key focus areas involve whole genome sequencing (de novo and re-sequencing), custom amplicon sequencing and metagenomics (viral and bacterial). The NICD Sequencing Core Facility currently supports The genomics server offers secure, powerful, and flexible bioinformatic computing accessible to all NICD scientists. CLC Genomics Server Core aims to provide a unique and stable software architecture core that makes it possible to apply a range of bioinformatics analysis-solutions on high-throughput sequencing data.

Specialized facilities and equipment in the Sequencing Core Facility

The sequencing core facility has a dedicated server (genomics server) for data analysis. The genomics server offers secure, powerful, and flexible bioinformatic computing accessible to all NICD scientists. CLC Genomics Server Core aims to provide a unique and stable software architecture core that makes it possible to apply a range of bioinformatics analysis-solutions on high-throughput sequencing data.

Equipment for molecular biology applications includes:

- three Illumina MiSeq sequencers
- Pacbio
- Illumina Nextseq 550
- Flurometric Quantitation: Qubit/Quant-iT `
- NanoDrop Spectrophotometer
- Agilent TapeStation
- FlashGel Electrophoresis System
- Standard Agarose Gel Electrophoresis
- MilliQ or Ultrapure Water System (18.2 MΩ-cm water)
- Heat block(s)
- Centrifuge:
- Microplate rotor
- Microcentrifuge rotors (for 1.5-20mL tubes)
- Thermal Cyclers
- Real-Time Thermal Cyclers
- Ultraviolet transilluminator with gel documentation system
- PAGE gel electrophoresis equipment

Specific competencies for sequencing core facility

Performing and analysing full genome or sequencing with next generation sequencing techniques.
Additional competencies:

- Library preparation: libraries are created using random fragmentation of DNA, followed by ligation with custom linkers
- Amplification: the library is amplified using clonal amplification methods and PCR.
- Sequencing: DNA is sequenced using one of several different approaches
- Analysis of sequence data

2. Training programme in molecular biology

2.1 Description of Training programme

Each intern medical scientist will complete a 2-year training program. The training program will comprise a minimum of 21 months in the host Centre. Core competencies are expected to be met by each intern. Each host Centre will additionally train in Centre specific competencies. There will be 2- 3 months of rotations in a different NICD Centre or as part of the established 3-month NICD annual rotation programme, when all laboratories at the NICD are visited for up to 2 weeks each.

2.2 Summary of training programme

A	21-22 months	Host centre at NICD	Any of the centres at NICD
B	2-3 months*	Rotation	Rotation programme through various NICD centres

*For the rotation through other NICD centres – a minimum of 4 other centres will be visited.
Rotation choice depends on workload and logistical considerations.
Choice will be determined by consultation between NICD staff and relevant laboratories.

2.3 Overall Outcomes of the internship:

2.3.1 To be able to recognise and apply professional conduct and ethical principles.
2.3.2 To be able to perform the administration and management of a laboratory in terms of maintaining the quality process, Good Laboratory Practice, laboratory safety and the quality management system)
2.3.3 To be able to apply basic scientific principles and academic knowledge.
2.3.4 To be able to perform laboratory methods in accordance with standard operating procedures and the interpretation of results relevant to a laboratory diagnostic environment.
2.3.5 To be able to define and apply research principles, compile a scientific report and present the findings. (Use of database/s and apply bioinformatics).

2.4 Outline of training programme during twenty-one-month program

The following general principles will be covered in the 21-month rotation.

- **Good Laboratory Practice**: Regular training is conducted for all staff. Laboratory divisions conducting patient testing have SANAS accreditation for ISO 15189. This will include exposure to laboratory management, quality assurance activities of the department, role of standard operating procedures and adherence to these, documentation such as quality manual, safety manual etc. This will involve an orientation program and ongoing bench exposure.
- **Safety Training –** regular training provided for all staff. The safety representative in the laboratory will be responsible for the training.
- **General Laboratory techniques:** centrifugation, pipetting, sample preparation, chain of custody, laboratory information system, sample storage.

The 21-month rotation will ensure that the intern emerges with expert knowledge in molecular biology, be able to troubleshoot as well as use initiative to instigate new work in a particular area. During this time, they will be expected to spend at least 50% of their time on routine work done by the laboratory. Research projects they are doing, including the possibility of a Masters project, should fit within the remaining 50% of time.

Each Centre will offer at least two modules to the intern scientist during the 21-month period. Intern scientists will be expected during this time to become proficient in running the routine assays carried out by their unit. They will become expert in the molecular assays including troubleshooting when there are problems, instrument maintenance and quality control measures. They will be expected to attend the academic teaching available in the unit e.g. tutorials, journal clubs etc. They will also attend the bi-monthly NICD research meeting. Interns maybe given an opportunity to present at university research days and/or national conferences, where possible.

The intern scientist will be expected to compile a portfolio suitable for assessment as determined by the HPCSA. This will include an information on all assays witnessed and performed as well as one or more projects. The project(s) may include at least one of the following

- Instrument validation
- Test validation
- Test optimisation
- Research question

With appropriate university or ethics approvals, if necessary.

2.5 Outline of training included in the 2-3 month modules

During the 2-3 month rotations, the intern will be exposed to the theory and techniques spanning the tests offered by the laboratory. The aim is to give an overview of tests available, equipment and expertise available, an introduction to the pathology tested in the various units, and to stimulate the interest of the intern. The intern will be expected to understand the principles involved in the techniques. They will NOT however be expected to have performed all the techniques mentioned, nor to be able to run the tests without supervision. Rather the aim is to learn which tests are available and for which patients they would be applicable.

3 Assessment

Assessment will be performed according to rules and regulations stipulated by the HPCSA. Requirements for internal assessment of the candidate will be the following:

3.1: Ongoing assessment

Ongoing assessment will consist of an evaluation report of the intern scientist by the unit head after a year of internship and finally before portfolio submission. The report will be based on the interim portfolio being collated by the intern (see below) as well as an evaluation of his/her general laboratory demeanour including:

- Attention to good laboratory practice
- Participation in academic activities
- Laboratory expertise acquired

The evaluation will be discussed in full with the scientist during an interview and relevant feedback given. Opportunities for improvement will be discussed and noted.

3.2: Final Portfolio

For registration in the discipline of Immunology, the portfolio will consist of:

- Logbook of tests performed
- Logbook of tests witnessed but not performed
- Printout of any oral presentations e.g. PowerPoints
- Copy of any journal articles presented with short explanation of for which forum it was presented e.g. "presented at immunology journal club, 27 January 2019" and signed by a senior staff member or the journal presenter.

- At least one of the following
    - **1. Project demonstrating capability in the scientific method and computer literacy. This may have the form of a research paper i.e. including introduction, methods, results, discussion, conclusion and references or in the form of an instrument or test validation and written up as a report.** These must comply with ethical guidelines and ethics approval must be included, if required, by the study. Dissemination of the results via conference presentation or publication is desirable.

    - **2. A case study related for which a molecular diagnostic test has been used, including patient history, clinical investigations, laboratory investigations, discussion and references**. These must comply with ethical guidelines and ethics approval must be included, if required, by the study. Dissemination of the results via conference presentation or publication is desirable.

- Evaluation reports/ attendance certificate from head of relevant units at the end of each rotation.

4 Competencies

The following are the specific competencies expected from all intern medical scientists on completion of internship in molecular biology:

4.1 Core laboratory Competencies in Molecular Biology

Core laboratory competencies expected from a scientist in molecular biology include the following:

- Perform DNA/RNA extraction

- Perform quantification and purity assessment of DNA/RNA/protein
- Perform a traditional PCR assay
- Interpret PCR results via gel electrophoresis
- Perform a real-time PCR assay
- Interpret results of a real-time PCR assay
- Ability to make up solutions using calculations of molar concentration and molecular weights
- Sequence assembly and application of general/ advanced tools to analyse data

4.2 Core theory for a scientist in Molecular Biology

Core theoretical knowledge for a scientist in molecular biology includes the following:

- Principles of cell biology and cell structure
- Principles of DNA replication, transcription, translation, cell division
- Understanding of nomenclature for triplet amino acid codes
- Principles of epigenetics
- Principles of molecular amplification techniques including PCR, isothermal amplification methods etc.
- Use of bioinformatics tools
- Principles of DNA sequencing
- Understanding of statistical concepts including sensitivity, specificity, positive and negative predictive values of laboratory assays.
- Principles for method evaluation and method comparison

4.3 Other Laboratory Competencies

- Ability to provide interpretation of molecular data and a diagnostic opinion
- Understanding of the molecular methodology advice
- Awareness of the evidence base that underpins the use of the procedures employed by the molecular laboratory
- Must be able to interpret data and recommend further course of action
- Must be aware of the strengths and weaknesses of the evidence base for commonly used procedures and investigations in molecular biology.
- Must be able to contribute to monitoring of patients as appropriate within molecular diagnostic service.
- Awareness of importance of turn-around times and audit trail to ensure quality of results

4.5 Technical Competencies

- Understanding of the principles associated with a range of techniques employed in the molecular biology specialty.
- Knowledge of the standards of practice expected from these techniques used in molecular biology
- Experience of performing techniques in molecular diagnosis.
- The ability to solve problems that might arise during the routine application of techniques (troubleshooting) used in molecular biology
- Understanding of the principles of quality control and quality assurance
- Experience of the use of quality control and quality assurance techniques including restorative action when performance deteriorates.
- Ability to perform common technical procedures in molecular biology as detailed in the local Standard Operating Procedures.
- A critical ability to review the results and determine the significance of quality control and assessment information for relevant analytical procedures in molecular biology

- A detailed understanding of analytical principles utilised in molecular biology to facilitate method troubleshooting and the development of adequate procedures of preventative maintenance.
- An understanding of the hazards (environmental, biological, chemical, radioisotopic) associated with the practice of molecular biology and the appropriate controlling legislation and appropriate procedures of risk assessment.

4.6 Scientific Competencies

- Understanding the science that underpins the molecular biology specialty
- Demonstrating a strong base of knowledge appropriate to the molecular biology specialty and to the investigations available.
- Experience of searching for knowledge, critical appraisal of information and integration into the knowledge base of molecular biology.
- Ability to make judgements on the effectiveness of procedures performed in molecular biology
- Application of the knowledge base to the molecular biology specialty and to the range of procedures/investigations available in molecular biology
- A critical understanding of the application of investigative protocols and diagnostic tests in the assessment of disease and disorders
- Critical understanding of the integration and interpretation of molecular biology parameters with other relevant diagnostic parameters
- Understand the principles of the techniques and methods employed in molecular biology
- Must be familiar with the evidence for, and limitations of, common molecular biology procedures used in the diagnosis
- A critical understanding of scientific method and the tools required to successfully evaluate, develop and/or modify both current and emerging technologies as routine diagnostic tools in molecular biology
- An understanding of sensitivity, specificity, positive and negative predictive values of an assay.

The following are the generic competencies expected from all intern medical scientists on completion of internship:

4.7 Research and Development Competencies

- Ability to read and critically appraise the literature ability to develop the aims and objectives associated with a project
- Ability to develop an experimental protocol to meet the aims and objectives in a way that provides reliable and robust data.
- Ability to perform the required experimental work ability to produce and present the results (including statistical analysis)
- Ability to critically appraise results in light of existing knowledge and the hypothesis developed and to formulate further research questions
- Ability to present data and provide a critical appraisal to an audience of peers – both spoken and written
- An awareness of the current extent of knowledge in immunology and an ability to employ appropriate information tools to search for, consolidate and critically examine information

4.8 Communication Competencies

- Ability to assess a situation and act accordingly when representing the specialty
- Ability to communicate the outcome of problem solving and research and development activities evidence of presentation of scientific material at meetings and in the literature
- Must be able to communicate effectively with professional colleagues within the discipline and in the wider scientific and clinical community
- Must be able to present findings effectively both orally and written

- Must be able to use modern communication devices

4.9 Problem Solving Competencies

- ability to assess a situation which may pose a problem
- ability to determine the nature and severity of the problem
- ability call upon the required knowledge and experience to deal with the problem
- initiate resolution of the problem
- demonstrate personal initiative
- must be able to interpret internal quality control and external quality assurance data
- must be able to recognise when a test or procedure is not within adequate performance limits
- must be able to recognise the consequences of inadequate performance of individual tests or procedures
- must be able to identify potential causes of problems and to investigate these appropriately
- must be able to identify and appropriate solution to the problem and propose an effective and timely solution, including any requirement for clinical follow-up

4.10 Management Competencies

- Understanding of the legal and ethical boundaries of scientific research.
- Ability to recognise the limits of personal practice and when to seek advice.
- Ability to manage personal workload and prioritize tasks appropriately.
- Understanding of the principles of clinical governance including importance of confidentiality, informed consent and data security clinical audit, accreditation requirements relevant to the virology specialty.
- The ability to contribute effectively to work undertaken as part of a multi-disciplinary team
- Ability to supervise others as appropriate to area of practice.
- Understanding of the role of appraisal in staff management and development.
- Understanding of the need for career-long self-directed learning and the importance of continuing professional development.
- Understanding of the need for, and ability to establish and maintain a safe practice environment.

understanding of the structure and organization of the department

4.11 Ethics and Values Competencies

- Apply and maintain appropriate professional ethics, values attitudes and behaviour.
- Use science and technology effectively and critically, showing responsibility towards the environment and health of others
- Understand and apply ethics in both human and animal research
- Understand and comply with the laws of copyright protection, confidentiality and ownership of intellectual property
- Take responsibility within own limits of competence and recognise the need for lifelong learning with an awareness of personal and knowledge limitations
- Recognise the ethical and legal aspects in the field including record keeping and documentation

Bibliography

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http://www.hpcsa.co.za/Uploads/editor/UserFiles/downloads/legislations/regulations/mdb/regulations/regulations_gnr_579_2009.pdf
REGULATIONS RELATING TO THE QUALIFICATIONS FOR REGISTRATION OF MEDICAL SCIENTISTS
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REGULATIONS RELATING TO THE REGISTRATION OF STUDENTS IN MEDICAL SCIENCE,
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REGULATIONS RELATING TO THE REGISTRATION OF CERTAIN CATEGORIES OF MEDICAL SCIENTISTS
http://www.hpcsa.co.za/Uploads/editor/UserFiles/downloads/legislations/regulations/mdb/regulations/regulations_gnr_52_97.pdf

Registration
http://www.hpcsa.co.za/ (registration forms may change, please use the most recent update)

Ethics and medico-legal aspects
HPCSA Guidelines on Ethical Rules (version available from the HPCSA website – Booklets 1 to 11)
https://www.hpcsa.co.za/Uploads/Professional_Practice/Ethics_Booklet.pdf
The general guidelines for health researchers and Biotechnology research in South African dealing with patients and patient samples (version available from the HPCSA website – Booklets 13 and 14).
https://www.hpcsa.co.za/Uploads/Professional_Practice/Ethics_Booklet.pdf
NHLS SOP GPL2773, Minimizing transcription errors, compliance checks….
NHLS SOP POLH0009, NHLS code of conduct
NHLS SOP CHE0599, GLP in a molecular laboratory
NHLS SOP IMM0201, GLP for immunology
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Safety and Quality Management
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Health and Safety Policies, NHLS POLS0003
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Potential Work Hazards, NHLS POLS0005
NHLS safety manual – hazardous biological agents, NHLS POLS0006
Safety and Waste Management forms, NHLS POLS0009
NHLS safety health and environment (SHE) policy, NHLS POLS0010
Part 2 - ISO 15189:2012 “Medical laboratories - Requirements for quality and competence”
https://www.westgard.com/iso-15189-2012-requirements-1.htm

Appendix 1

Evaluation Report – Intern Scientist

Name of intern scientist:…….
HPCSA no……
Name of supervisor……..
HPCSA no……
Position…….
Date:……
The intern scientist has been under supervision by the supervisor
from…… until……. in the ……laboratory.
The supervisor has found the intern scientist's performance in the following categories to be:

	1 good	**2 satisfactory**	**3 needs further training**
Processing routine samples:			
Working under pressure			
Working as part of a team			
Punctuality			
Enthusiasm			
Understanding scientific principles of diagnostic tests			
Understanding clinical impact of diagnostic test results			
Following the principles of good quality assurance			
Conducting research projects			
Presenting data to a scientific forum			
Troubleshooting laboratory assays			

Is the supervisor aware of any patient/doctor/customer complaints that resulted from the actions of the intern scientist? If so please provide details.
……
……
Is the supervisor aware of any laboratory results of poor quality issued by the intern scientist?
……
……
Are there specific areas in which the intern scientist excelled?
……
……
Areas for improvement?
……
……
Does the supervisor have any reservations about the intern scientist registering as a biological scientist with the HPCSA upon completion of the necessary requirements?

……(yes/no)

Signature…… (intern scientist)

Date……

Signature……..(supervisor)

Date……

Appendix 2:

Supervisor(s):			
Centre for Vaccines and Immunology (CVI)	Dr. Melinda Suchard	melindas@nicd.ac.za	011-3866387
Centre for Vaccines and Immunology (CVI)	Dr. Nishi Prabdial-Sing	niship@nicd.ac.za	011-3866347
Centre for HIV & Sexually Transmitted Infections (CHIVSTI)	Prof Adrian Puren	adrianp@nicd.ac.za	011-3866328
Centre for Respiratory Diseases and Meningitis (CRDM)	Dr. Mignon du Plessis	mignond@nicd.ac.za	011-5550387
Centre for Enteric Diseases (CED)	Dr. Anthony Smith	anthonys@nicd.ac.za	011-5550348