

Medical Scientist - Intern Training Programme – Virology
National Institute for Communicable Diseases

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 Virology 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 and Zoonotic Diseases (CEZD), Centre for HIV and STI (CHIVSTI), Centre for Respiratory Diseases and Meningitis (CRDM).

1.2 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) and measles. Specialized molecular diagnostic services are offered to South African stakeholders for Hepatitis B and Hepatitis C. The centre leadership comprises Dr Melinda Suchard (administrative head and immunology lead), Dr Nicky Gumede (polio lead), Dr Nishi Prabdial Sing (hepatitis lead), Sheilagh Smit (measles lead).

For the understanding of virological techniques and skill, the Centre divides its teaching and training program in three essential parts:

1.2.1. Laboratory technique: Cell Culture

The following sterile techniques are performed in Cell Culture and intern scientists will be trained on:

- Maintenance of cell lines
- Trypsinisation of Continuous cell lines
- Cell Counts and viability
- Bacterial control testing
- Preservation of cell lines
- Thawing/Resuscitation of cell lines
- Prevention of contamination of cell lines

1.2.2. Laboratory technique: Polio Serology/ Measles Serology and polio virus Isolation

Intern scientists usually visit the laboratory for a week. This makes it impractical for performance of lab techniques; however they are allowed to observe procedures performed at the time of training. Intern scientists must read and acknowledge the following lab specific SOPs in order to achieve a better understanding of lab procedures – specific acknowledgment forms to be completed for reference purposes.

Procedures to be discussed

Polio Serology:

1. Principle of the polio antibody neutralization test
2. Interpretation of results

Measles Serology:

Detection of measles-specific IgM antibodies

Polio Virus Isolation:

1. Sample receipt and processing
2. Virus isolation procedure
3. Interpretation of virus isolation results
4. Principle of virus neutralization assays and interpretation of results

1.2.3. Laboratory technique: CVI Molecular Virology

Intro to PCR and Real-time PCR, Introduction to sequencing and Gel electrophoresis

Understanding Quantitative tests, Alternative viral load assays, DISA training

HBV Training PCR (Automated extraction, Nested conventional PCR and Gel electrophoresis)

HCV genotyping by Sequencing and Line Probe assay (LiPA)

1.3 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 track record 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. The Centre for HIV & STIs leadership team consists of Professor David Lewis (Administrative Centre Head, STI section lead), Professor Lynn Morris (HIV Research section lead), Professor Adrian Puren (HIV Sero-Molecular Diagnostics section lead) and Professor Caroline Tiemessen (Cell Biology section lead) amongst others.

1.3.1 Support for HIV vaccine trials- HIV Serology and Molecular Virology

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

Laboratory Technique:

Manual ELISA IgM and IgG

Automated ELISA

ELISA antigen (eg. p24, HBsAg)

IgG avidity assays

Rapid tests

Western Blot

Validation of serologic assays

HIV-1 DNA PCR training and competency (Fully automated Qualitative PCR)

HIV-1 Viral load training and competency (Fully automated Quantitative QS PCR)

1.3.2 HIV drug resistance surveillance

HIV drug resistance testing- phenotypic and genotypic

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 2 softwares, Sequencher Version 5 and ReCall.

Interpretation of HIV-1 drug resistance report from the Stanford database.

DNA manipulation competencies:

Perform plasmid DNA extraction

Perform site-directed mutagenesis PCR

Endonuclease restriction and DNA ligation

Interpret PCR and restriction results with agarose gel electrophoresis

Bacterial transformation (includes growing bacteria on agar plates and liquid broth)

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

1.4. Centre for Enteric Diseases

The virology division of the Centre for Enteric Diseases (CED) aims to conduct surveillance and research on viruses associated with gastroenteritis. The division participates in a sentinel surveillance program at five sites around South Africa to monitor rotavirus epidemiology, genotype distribution and the impact of the rotavirus vaccine introduced into the expanded program on immunization (EPI) in August 2009. The division is also involved in investigating methods to improve vaccine safety and efficacy in developing countries. Furthermore, the division monitors the incidence, seasonality and molecular character of additional enteric viruses including, but not limited to, norovirus, sapovirus, adenovirus, astrovirus, bocavirus in children less than five years of age. The division also provides diagnostic support to the outbreak investigation unit.

Laboratory Technique:

Manual ELISA (Rotavirus detection)

Rapid tests (Rotavirus and adenovirus detection)

Automated extraction of viral nucleic acids

RT-PCR detection and genotyping of rotavirus strains

Real time RT-PCR detection of enteric viruses

1.5. Centre for Emerging and Zoonotic Diseases (CEZD), Special Viral Pathogens Laboratory (SVPL) (SPU) and Electron Microscopy (EM)

The Centre for Emerging Zoonotic Diseases (CEZD) aims to be a national and international centre of excellence for emerging and re-emerging zoonotic diseases. CEZD 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 CEZD supports South Africa's commitment to the International Health Regulations.

Laboratory Technique (SVPL) :

The following techniques will be discussed and demonstrated (when possible) due to biosafety issues related to laboratory handling of haemorrhagic fever virus, rabies virus and arboviruses. The CEZD operates multiple biosafety level 3 laboratories and the only biosafety level 4 laboratory in South Africa. These In addition the Centre operates several biosafety level 2 laboratories.

- Performing and analyzing molecular detection protocols for diagnosis of viral haemorrhagic fevers, rabies and arboviral infection including the use of real time, conventional and isothermal amplification protocols.
- Protocols for the detection of complete, IgG and IgM antibodies for diagnosis of viral haemorrhagic fevers, rabies and arboviral infection (including ELISA, indirect immunofluorescence analysis, haemagglutination inhibition assays and virus neutralization assays)
- Protocols for isolation of live virus from clinical specimens using cell culture and/or suckling mice for diagnosis of viral haemorrhagic fevers, rabies and arboviral infection

Laboratory Technique (EM);

Techniques and applications of conventional Transmission Electron Microscopy in virology.

1.6. Centre for Respiratory Diseases and Meningitis, Influenza

The Centre for Respiratory Diseases and Meningitis (CRDM) is a resource of 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, health care providers, regional and international collaborators, to assist with the planning of public health policies and programmes and response to respiratory disease and meningitis outbreaks. The CRDM is also a source of capacity building and formal training within South Africa and the African region.

Laboratory Technique:

Respiratory Virus propagation techniques in cell cultures

Immunofluorescence

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 microneutralization assays.

Pseudovirion-based microneutralization 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

Virus discovery for unknown causes of respiratory disease

Genome sequencing using both Sanger and next generation sequencing methods

1 Intern Training Program

2.1 Description of Training programme

Each intern medical scientist will complete a 2 year training program, unless special circumstances lead to the HPCSA accepting a shorter training period (such as the candidate already having completed a masters degree – see special case below). The training program will comprise 18 months in the host centre (either Centre for Vaccines and Immunology or Centre for HIV and STI). There will be a 6 month rotation through the other centres at the NICD.

We have capacity to train three interns per centre. Thus, at this point in time, with the Centres for Vaccines and Immunology and the Centre for HIV and STI able to train interns, we have capacity to train 6 intern scientists in virology at any one time.

2.2 Summary of training programme

A	18 months	Host centre at NICD	Centre for Vaccines and Immunology/ Centre for HIV and STI
	6 months	Rotation (2-6 weeks per other centres)	Centre for Enteric Diseases Centre for Zoonotic Diseases Centre for Respiratory Diseases and Meningitis Centre for Vaccines and Immunology/ Centre for HIV and STI

2.3 Outline of training programme during eighteen month program

The following general principles will be covered in the 18 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 18 month rotation will ensure that the intern emerges with expert knowledge in a particular field, 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 18 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 clinical indications for the assays, other testing

available for related conditions, requirements and pitfalls of the assays, instrument maintenance and troubleshooting. They will be expected to attend the academic teaching available in the unit eg:

- 2-weekly NICD research meeting
- 2-weekly journal club in Centre for Vaccines and Immunology
- Monthly talk given by invited speakers – Centre for Vaccines and Immunology
- Monthly journal club – Centre for HIV and STI

There are also a selection of optional courses from which to choose including

- All CEU courses offered by NHLS (booklet available)
- Research related courses offered by collaborating universities

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

- Instrument validation

test validation

test optimisation

research question

with appropriate university or ethics approvals if necessary.

2.4 Outline of training included in the rotation period

During the 6 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 at the end of each rotation completed (ie the end of each month rotation, and twice during the 18 month host stay). 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
- Personal interaction with other staff members

The evaluation report will be discussed in full with the scientist during an interview and relevant feedback given. Opportunities for improvement will be discussed and noted. A hard copy of the report will be placed in the intern's portfolio.

3.2: Final Portfolio

For registration in the discipline of **Virology**, the portfolio will consist of:

- logbook of tests performed
- logbook of tests witnessed but not performed
- print out of any oral presentations eg. powerpoints given
- copy of any journal articles presented with short explanation of for which forum it was presented eg “presented at virology journal club, 27 January 2013” and signed by a senior staff member.
- minimum of one project demonstrating capability in the scientific method and computer literacy. This may have the form of a research paper ie including introduction, methods, results, discussion, conclusion and references or a instrument/test validation report (including background, intra-run precision, inter-run precision, accuracy and references)
- Evaluation reports from head of relevant units at the end of each block, indicating strengths and areas for improvement.
- Log of any complaints received or corrective actions undertaken with regards to errors in specimen processing or communication.

4. Special cases

4.1 Six month internship period

This rotation will be applicable to those candidates already in possession of a Masters degree, or other circumstances as dictated by the HPCSA. In this case the intern will complete 2 X 3-month long modules in the Centres for Vaccines and Immunology and Centre for HIV and STI. The intern will be expected to comply with HPCSA rules and regulations comprising full registration. For internal assessment, the requirement for a research component in their portfolio will be waived. Additionally they will only require two evaluation reports in their final portfolio.

4.2 Concurrent registration in Virology and Molecular Biology

In the case of an intern wanting to register in two categories, for example Virology and Molecular Biology, it will be expected that they meet the assessment criteria for both disciplines. This involves submitting a final portfolio that meets the criteria for a Virology portfolio as well as a Molecular Biology portfolio. The research project(s) done should be applicable to both disciplines.

5. Competencies

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

5.2 Technical Competencies

- understanding of the principles associated with a range of techniques employed in the various

virology specialities.

- knowledge of the standards of practice expected from these techniques used in virology
- experience of performing techniques in virological diagnosis/surveillance, by understanding and following of SOPs.
- the ability to solve problems that might arise during the routine application of techniques (troubleshooting) used in virology
- 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.
- a critical ability to review the results and determine the significance of quality control and assessment information for relevant analytical procedures in virology
- an understanding of the hazards (environmental, biological, chemical, radioisotopic) associated with the practice of virology and the appropriate controlling legislation and appropriate procedures of risk assessment.

5.3 Scientific Competencies

- Understanding the science of virology and the broader aspects of medicine and clinical practice.
- experience of searching for knowledge, critical appraisal of information and integration into the knowledge base of virology.
- ability to apply knowledge to problems associated with the routine provision, and development, of the service
- ability to identify the clinical decision which the test/intervention will inform
- ability to make judgements on the effectiveness of procedures performed in virology
- application of the knowledge base to the virology specialty and to the range of procedures/investigations available in virology
- a critical understanding of the application of investigative protocols/ diagnostic tests/surveillance testing used in virology
- understand the principles of the techniques and methods employed in virology
- able to advise on appropriate choice of investigation and sample preparation
- must be familiar with information on technical developments and emerging technologies in virology
- a critical understanding of classification criteria for viruses
- An understanding of sensitivity, specificity, positive and negative predictive values of an assay and how these are affected by prevalence of a disease.

5.4 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 the 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

- developed research skills and expertise sufficient to support supervised and collaborative research initiative in haematology
- an awareness of the current extent of knowledge in virology and an ability to employ appropriate information tools to search for, consolidate and critically examine information
- participation in local research meetings and supervised and collaborative research initiatives, leading to in-house reports (eg validation reports), publications or a research Masters degree
- self-endeavour (eg literature awareness) under the tutelage of an appropriate virology specialist.

5.5 Communication Competencies

- ability to assess a situation and act accordingly when representing the specialty
- ability to respond to enquiries regarding the service provided when dealing with clinical colleagues
- ability to communicate with patients, carers and relatives, the public and other healthcare professionals as appropriate
- 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 in a variety of written and spoken media must be able to educate and train professional colleagues within and without the department
- must understand the requirements and responsibilities associated with the supervision of junior colleagues
- must be able to use modern communication devices
- must understand basic management techniques and be aware of topical management issues

5.6 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

5.7 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

5.8 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
- demonstrate an ability to work as a team and to show respect for colleagues and other health care professionals and the ability to foster a positive collaborative relationship with others.
- recognise the ethical and legal aspects in the field including record keeping and documentation
- flexibility to adapt to uncertainty and change