

Intern Scientist Training Programme – Immunology
National Institute for Communicable Diseases

Compiled by Dr Melinda Suchard, June 2013

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.

1.2 Background to the 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).

1.2.1 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 polio virus. 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 polio viruses (VDPVs).

The Centre for Vaccines and Immunology is a national and World Health Organisation accredited regional referral laboratory for AFP surveillance. The centre conducts polio virus isolation, identification and molecular analysis for South Africa, Angola, Botswana, Lesotho, Mozambique, Namibia, Swaziland, Angola and the Democratic Republic of Congo. 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 Organisation. Results are also given to clinicians treating the patients.

1.2.2 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 Millenium 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 Organisation for measles. The centre also uses PCR and sequencing to genotype measles strains and analyse the phylogenetic trees for any measles outbreak. Molecular epidemiology provides information to authorities regarding geographic distribution and evolution of measles strains.

Since rubella presents with similar clinical symptoms, laboratories often test for IgM against both viruses in suspected measles cases. Rubella surveillance projects have been run by the centre and future rubella surveillance is planned.

1.2.3 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. There is no national surveillance program for hepatitis B. The Centre for Vaccines and Immunology provides a diagnostic service for hepatitis B, releasing results to referring clinicians. Additionally the centre performs genotyping to identify circulating strains of hepatitis B. Any positive sera from the South African National Blood Service are also genotyped by the centre. Genotyping results are interpreted together with serological testing results. Genotyping gives a snapshot of the burden of disease caused by each strain.

1.2.4 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 diagnostic testing for hepatitis C, reporting results to referring clinicians. The centre also performs genotyping to identify the strain. Strain information provides prognostic information to the clinician. Additionally the centre performs genotyping for any positive hepatitis sera from the South African National Blood Service.

1.2.5 Immuno-regulation laboratory

The immuno-regulation laboratory in the centre aims to identify correlates of protection to Tuberculosis and other infectious diseases by characterising 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.

1.3 Background to the 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 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 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.

1.3.2 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 paediatric 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.

1.3.3 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

1.3.4 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.

1.3.5 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.

1.3.6 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).

1.3.7 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.

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 3 month rotation through the other centre at the NICD. There will be an additional 3 month rotation through a different collaborating NHLS or NICD laboratory (Examples include Immunology laboratory, Tshwane; Immuno-haematology laboratory, NHLS Charlotte Maxeke; Immunology laboratory, NHLS Tygerberg, other centre at NICD). Choice depends on preference of the intern, travel logistics and workload of the laboratory at the time. This rotation will ensure that the intern is exposed to many facets of immunology and masters many applicable techniques as well as becomes familiar with the clinical conditions and pathology related to many clinical tests.

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 immunology at any one time.

2.2 Summary of training programme

A	18 months comprising 2 X 9 months	Host centre at NICD	Centre for Vaccines and Immunology Centre for HIV and STI
	9 months	Host centre at NICD	Laboratory 1 (eg measles/polio/hepatitis/drug resistance/STI/incidence)
	9 months	Host centre at NICD	Laboratory 2 (eg measles/polio/hepatitis/drug resistance/STI/incidence)
B	3 months	Alternate centre at NICD	Centre for Vaccines and Immunology Centre for HIV and STI
C	3 months	Other NICD or NHLS laboratory conducting immunology testing	For example, but not limited to, Immuno-haematology Charlotte Maxeke, Immunology Tygerberg, Immunology Tshwane; Immunology Cape Town; Centre for Respiratory Diseases and Meningitis, Centre for Opportunistic, Tropical and Hospital

			infections, Centre for Enteric Disease, Centre for Tuberculosis, Centre for Emerging and Zoonotic Diseases
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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
- 2 week course in Basic and Advanced Immunology run by the Centre for Vaccines and Immunology and the University of the Witwatersrand
- Weekly journal club in immunology offered at University of the Witwatersrand in collaboration with the Centre for Vaccines and Immunology

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 3 month modules

During the 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 at the end of each rotation completed (ie the end of each 3 month rotation, and twice during the 18 month module at the end of each 9 month rotation). 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 **Immunology**, the portfolio will consist of:

- logbook of tests performed
- logbook of tests witnessed but not performed
- printout 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 haematology 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)

- a minimum of two case studies, related to an immunological condition, including patient history, patient examination, clinical investigations, laboratory investigations, discussion 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 Immunology and Molecular Biology

In the case of an intern wanting to register in two categories, for example Immunology 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 an Immunology 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:

5.1 Clinical Laboratory Competencies

- ability to provide interpretation of immunological data and a diagnostic opinion, including any further action to be taken by the individual directly responsible for the care of the patient
- understanding of the wider clinical situation relevant to the patients presenting
- ability to develop/devise an investigation strategy taking into account the complete clinical picture
- understanding of the clinical applications of immunological methodology and the consequences of decisions made upon his/her actions/advice
- awareness of the evidence base that underpins the use of the procedures employed by the immunological laboratory

- must understand the underlying mechanisms of the pathology of immunological disease
- must be able to advise on choice of investigation in immunological diseases
- must be able to interpret data and recommend further course of action within the wider context of the clinical situation.
- must be able to relate data from other disciplines to the overall clinical situation.
- must be aware of the strengths and weaknesses of the evidence base for commonly used procedures and investigations in immunology.
- must be able to contribute to monitoring of patients as appropriate within immunology diagnostic service.
- Awareness of importance of turn-around times and audit trail to quality of results

5.2 Technical Competencies

- understanding of the principles associated with a range of techniques employed in the immunology specialty.
- knowledge of the standards of practice expected from these techniques used in immunology
- experience of performing techniques in immunological diagnosis.
- the ability to solve problems that might arise during the routine application of techniques (troubleshooting) used in immunology
- 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 haematology 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 immunology
- a detailed understanding of analytical principles utilised in immunology 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 immunology and the appropriate controlling legislation and appropriate procedures of risk assessment.
- Adequate numbers of samples run involving various techniques relevant to the discipline and subspecialty (eg involving use of a log book recording practical experience in the relevant haematology unit)

5.3 Scientific Competencies

- understanding the science that underpins the immunology specialty and the broader aspects of medicine and clinical practice.
- demonstrating a strong base of knowledge appropriate to the haematology specialty and to the investigations and therapeutic options available.
- experience of searching for knowledge, critical appraisal of information and integration into the knowledge base of haematology.
- 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 immunology
- application of the knowledge base to the haematology specialty and to the range of procedures/investigations available in immunology

- a critical understanding of the application of investigative protocols and diagnostic tests in the assessment of immunological disorders
- critical understanding of the integration and interpretation of immunological parameters with other relevant diagnostic parameters in the overall clinical assessment of the patient
- understand the principles of the techniques and methods employed in immunology
- able to advise on appropriate choice of investigation and sample preparation
- must be familiar with the evidence for, and limitations of, common immunological procedures used in the diagnosis and management of patients
- must have a basic knowledge of related disciplines in order to be able to integrate relevant diagnostic results into an interpretation
- must be familiar with information on developments and needs in immunology
- 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 haematology
- a critical understanding of classification criteria for immunological disease entities
- a critical understanding of diagnostic criteria in determining disease prognosis and outcome in immunology.
- An understanding of sensitivity, specificity, positive and negative predictive values of an assay and how these are affected by prevalence of a disease.
- secondment to immunology specialist units where appropriate.

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 immunology 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 immunology 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 the Immunology specialty, and the ethical aspects 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 haematology 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