

## Respiratory Virus Unit

### BACKGROUND

The Respiratory Virus Unit (RVU) along with the Virus Isolation laboratory, comprise the WHO National Influenza Centre (NIC) at NICD and are involved in isolating and characterizing circulating influenza strains throughout many parts of South Africa. The epidemiologic and virological data collected through the Viral Watch Surveillance program is shared with the WHO Global Influenza Surveillance Network. This data contributes to the annual influenza vaccine update for each southern hemisphere winter season.

In recent years, the increasing spread of Highly Pathogenic Avian Influenza (HPAI) H5N1 subtype has highlighted the need for pandemic preparedness. The RVU has been involved in strengthening such preparedness by participating in rapid response outbreak training for avian and pandemic influenza throughout South Africa as well as facilitating capacity building for the rapid molecular detection of avian and seasonal influenza subtypes in Southern Africa

### ACTIVITIES, HIGHLIGHTS AND ACHIEVEMENTS

#### SEASONAL INFLUENZA

During the 2008 winter season, 441 influenza isolates were made, of which 345 (78%) were subtyped as H1N1 and fourteen isolates as H3N2. Virus strains from both influenza B lineages were detected; 44 from B/Yamagata/16/88 and 11 from B/Victoria/2/87. Twenty seven samples were untyped (12 influenza B isolates and 15 influenza A isolates).

Genetic drift away from the vaccine strains was determined by partial sequencing of the HA1 subunit of the haemagglutinin (HA) gene. Phylogenetic analysis of the H1N1 viruses showed that genetic drift away from the vaccine strain, A/SolomonIslands/3/2006, had been observed. The South African strains were shown to cluster within clade 2B which was characterized by the reference strain A/Brisbane/59/07.

Phylogenetic analysis of the subtype H3N2 strains revealed that the South African isolates clustered with the vaccine virus, A/Brisbane/10/07. Amino acid changes at position 173 distinguished three subgroups, two of which were characterized by A/Johannesburg/5/2008 (K173Q) and A/Johannesburg/15/08

(K173N, 3L5, K83N and L157S). The third subgroup, of lesser prominence, was identified by A/Wisconsin/3/2007 (K173E). Phylogenetic analysis of NA gene revealed genetic drift, with additional changes being identified in A/Johannesburg/15/2008.

The viruses isolated from the B/Yamagata/16/88 lineage were similar to those isolated during 2007. Three clades were identified, two of which were represented by the vaccine strains B/Florida/4/2006 and B/Brisbane/3/2007. The viruses isolated from the B/Victoria/2/87 lineage were also similar to those isolated in 2007.

This season saw the emergence of antiviral drug resistant H1N1 strains. Resistance to the antiviral drug, oseltamivir, was conferred by a single point mutation, H275Y, at the active site of the neuraminidase gene. A phenotypic assay, the enzyme inhibition assay, was performed by the WHO Collaborating Centres for Reference and Research in Melbourne and London on a number of South African isolates and the genotypic assay, a PCR based detection method, was performed by the RVU on the South African H1N1 isolates. 100% of the H1N1 isolates in South Africa were shown to be highly resistant to oseltamivir during 2008. Phylogenetic analysis of the NA gene revealed that the South African isolates fell within the 'European' cluster which belonged to clade 2B. The H1N1 samples remained sensitive to the antiviral drug zanamivir.

During the WHO Consultation on the Composition of Influenza Vaccine for the Southern Hemisphere held in September 2008 it was decided that the H1N1 subtype was to be updated due the antigenic drift observed during the current season. The recommended composition of influenza virus vaccines for the 2009 influenza season is A/Brisbane/59/2007 (H1N1)-like virus, A/Brisbane/10/2007 (H3N2)-like virus and B/Florida/4/2006-like virus

#### PANDEMIC PREPAREDNESS

The laboratory participated in external quality assurance panels provided by WHO and QCMD. These panels are designed for the rapid identification of seasonal and avian influenza subtypes by molecular detection techniques.

The RVU continued their role in avian and pandemic influenza preparedness by participating in the provincial 'Rapid Response Outbreak Training for Avian/Pandemic Influenza' carried out jointly by NICD

and Department of Health. The training was completed in the first quarter of 2008. Thereafter, Jack Manamela attended the Influenza Pandemic desk top exercise held in Benoni, Johannesburg from 16-17 October 2008. The objectives of the meeting were to raise awareness of an influenza pandemic and its impact on South Africa, to understand the key requirements for preparedness measures and to plan for additional requirements to support national pandemic preparedness actions.

RVU hosted laboratory technicians and scientists from the National Influenza Centre in Dar es Salaam, Tanzania and the Instituto Nacional de Saúde Publica, Luanda, Angola in February and May respectively. They were trained on molecular techniques to rapidly detect seasonal and avian influenza viruses. The unit also participated in a training course on the detection and subtyping of influenza viruses by real time PCR hosted at NICD from 29 September 2008 to 1 October 2008. The course was run by Dr Stephen Lindstrom from the Influenza Division at CDC, Atlanta and included participants from various African countries.

RVU has provided support to influenza laboratories in SADC countries by supplying reagents for molecular testing and providing technical advice.

## CAPACITY BUILDING

NICD hosted the annual influenza symposium for the Viral Watch doctors from 25-26 February 2008. The participants were introduced to virus isolation and molecular characterization techniques during a laboratory tour organized by RVU and the Virus Isolation Unit.

Dhamari Naidoo visited the University Teaching Hospital in Lusaka, Zambia as part of a CDC mission to strengthen regional laboratory capacity for influenza in January 2008. Amelia Buys, the senior technologist from the Virus Isolation Unit visited the Diagnostic Influenza Division at CDC, Atlanta from 24 March 2008 to 25 April 2008. She received training on influenza virus microneutralization assays, immunofluorescence assays, hemagglutination inhibition assays and virus isolation techniques.

The unit also participated in various meetings throughout the year. Jack Manamela attended the Sentinel Surveillance meeting held in Entebbe Uganda from 11-13 March 2008. The objectives of this meeting were to develop capacity for the monitoring and detection of seasonal and avian influenza strains in the WHO AFRO region. Dr Besselaar attended a CDC Influenza Cooperative Agreements Workshop which was held from 13-15 August 2008 in Cairo, Egypt. Dhamari Naidoo gave presentations at the Wits Research Day on 20 August 2008 and the NICD Academic day on 11 November 2008 on the emergence of oseltamivir resistant H1N1 strains. Dhamari Naidoo also participated in a WHO meeting with National Influenza Centres on strengthening the Global Influenza Surveillance Network held in Barcelona, Spain from 2-5 December 2008.

The unit bid farewell to Dr Besselaar who joined the WHO Global Influenza Program in Geneva in November 2008.



**Professor Barry Schoub presenting Dr Terry Besselaar with a certificate for 25 years of service, prior to her departure for Geneva.**