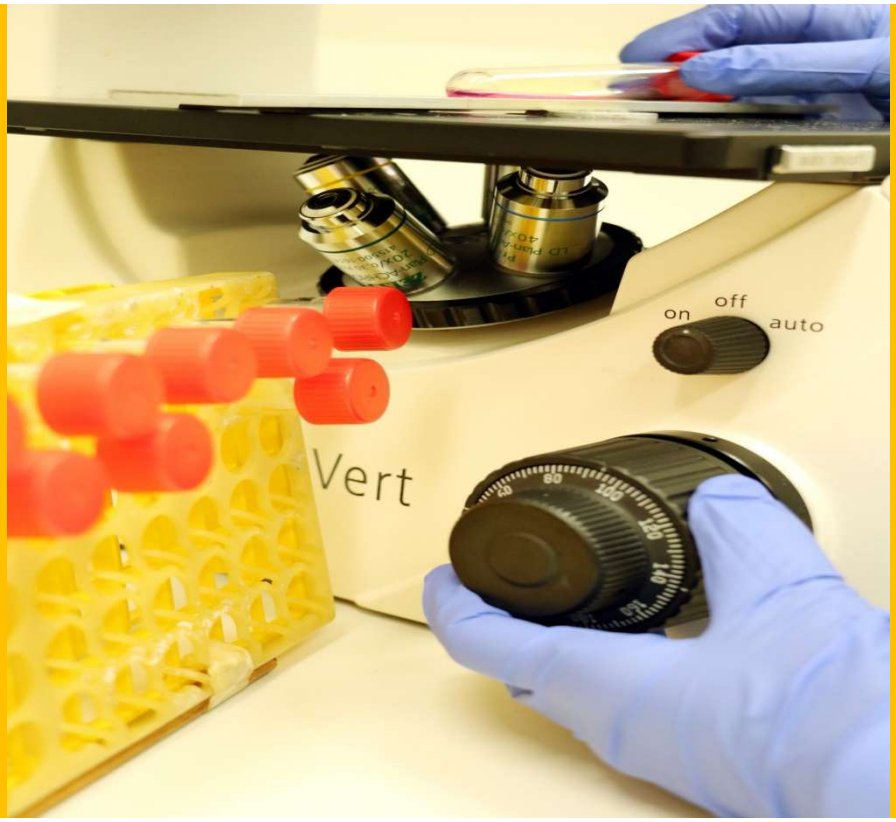
Measles Molecular Epidemiology:

Australia 2018



Victorian Infectious Diseases Reference Laboratory

Summary Report

VIDRL
Victorian Infectious Diseases Reference Laboratory

Doherty Institute
A joint venture between the University of Melbourne and the Royal Melbourne Hospital

1. Background

The measles and rubella laboratory at the Victorian Infectious Diseases Reference Laboratory (VIDRL) serves as the National Reference Laboratory for Australia and a WHO Regional Reference Laboratory for the Western Pacific Region. This laboratory provides a reference service for the detection and molecular genotyping of measles and rubella virus strains as part of its National Reference Laboratory function. Important aspects of laboratory molecular surveillance of measles and rubella at VIDRL during the post elimination phase include (i) genetic characterisation of circulating wild-type viruses to determine transmission events/pathways and support molecular epidemiological studies; (ii) differentiating vaccine strains from wild-type virus during outbreaks and (iii) monitoring the absence or persistence of endemic measles and rubella transmission.

Following a retrospective molecular epidemiological survey of Victorian measles strains from 1973-1998 (at the time the world's largest), VIDRL's measles molecular surveillance from 1999 indicates that measles transmission has been interrupted within Australia. Measles molecular epidemiological surveillance is widely accepted as a key criterion demonstrating the absence of an endemic genotype, and helping to demonstrate that a high proportion of cases and outbreaks are imported. VIDRL's work has improved understanding of the global distribution of measles genotypes by defining those from source countries that were imported into Australia, and has identified three previously undescribed measles genotypes. Optimal periods for measles virus RNA recovery from specimens have been defined, together with validation of nucleic acid based measles detection direct on patient samples specifically for the measles vaccine strain and/or subsequent genotyping.

More recently, genotyping evidence played an important role in verifying the interruption of endemic rubella virus in Australia for the years 2012 to 2017, one of the few countries in the region to have achieved this milestone. Australia was also successful in maintaining its measles elimination status for 2017 with genotyping evidence continuing to support the absence of endemic measles transmission.

This annual report provides a comprehensive description on the molecular epidemiology of measles and rubella in Australia for year 2018 and provides virological evidence supporting the sustained interruption of endemic transmission, of both measles and rubella viruses, in 2018.

2. Measles Molecular Epidemiology Australia, 1 January to 31 December 2018

The number of samples tested for measles RNA by real-time PCR during the reporting period was 800, an increase of 12% over the previous year. Of these, 106 (13.6%) samples had measles virus RNA detected from 84 cases. A measles genotype was obtained from 80 cases of which 62 were wild-type strains and 18 vaccine strains (Table 1). The remaining 4 cases had an RNA copy number that was too low (Ct>38) for genotyping (untypable).

From a minority of jurisdictions with local measles genotyping capabilities, fifteen N450 sequences were submitted to VIDRL or MeaNS for inclusion in the national database and are included in this report.

Wild-type measles cases were detected in 34 of the 52 reporting weeks (Figure 1) with circulation detected in six Australian States and one Territory (Figure 2). At least 46 known importation events from 13 countries or regions were identified as possible sources (Figure 3-4). Only 2 wild-type measles genotypes, B3 and D8, were identified during this period. In Australia, genotypes identified reflects the source of imported virus which is consistent with genotypic patterns seen in countries that have eliminated measles.

Genotype D8, the most common type detected (n=51), circulated following at least 31 separate cases were imported from foreign countries. This genotype was predominately introduced into Australia from India, Indonesia and Thailand. Other source countries/regions included Brazil, Lebanon, Myanmar, Philippines, Vietnam and South East Asia (Figure 3). The measles genetic lineage for the majority of these genotype D8 cases identified in Australia could be matched to a named strain or to a genetic viral strain found in other parts of the world with the nucleotide sequence often consistent with the source country of importation (Figure 5). Osaka, Hulu Langat, Victoria and Gir Somnath are all named strains identified in 2018 (Figure 5, Table 2). For the very small number of cases with no exact N450 sequence match in MeaNS, epidemiologic data indicated a known imported primary case. The weekly distribution of measles genotype D8 grouped by phylogenetic clustering (Figure 3) clearly shows the absence of an endemic genotype lineage, providing

strong evidence that Australia has sustained the interruption of endemic measles transmission of this genotype in 2018. Furthermore, phylogenetic analysis of outbreaks caused by measles genotype D8 in Australia (Figure 7A, 7D-7J), where available, supports a single viral lineage consistent with a single transmission chain for the small number of cases per outbreak. The largest of the measles D8 outbreaks occurred in Western Australia and was comprised of 10 cases following importation from Indonesia. Only 7 samples were available for measles genotyping from which genotyping was obtained from 4 cases (Figure 7G).

There were 26 cases of measles genotype B3, with epidemiologic and genetic data consistent with imported or imported-related virus (Figure 4, 7). Introduction of this genotype originated from Afghanistan, Malaysia, Pakistan, United Arab Emirates and Philippines. However, most introductions into Australia were from the Philippines where this genotype remains endemic (Figure 4). Most B3 cases were linked to one of two Gombak named strains while others were related to the Kabul named strain and the Harare named strain. All of the remaining genotype B3 non-named strains had exact N450 sequence match to other geographical strains found in MeaNS (Figure 6). As with the genotype D8s identified in Australia, the weekly distribution of measles genotype B3 grouped by phylogenetic clustering (Figure 4) provides solid evidence that Australia has sustained the interruption of endemic measles B3 transmission in 2018. The phylogenetic analysis of measles B3 outbreaks in Australia (Figure 7B-7C) supports this elimination claim with the largest B3 outbreak occurring in Victoria and consisted of only 9 cases after being imported from Malaysia (Figure 7C).

Table 1 and Table 2 provides a de-identified line-listing of measles vaccine cases and wild-type measles genotyping data by state and territory, virus lineage and WH0 representative strain, respectively.

3. Rubella Molecular Epidemiology Australia, 1 January to 31 December 2018

In 2018, 282 specimens were referred to VIDRL for rubella nucleic acid testing of which only 1 was positive for rubella virus RNA by the rubella real-time PCR. Phylogenetic analysis of 739 nucleotides of the rubella E1 protein identified the virus to be a rubella genotype 2B (Figure 8). This Western Australian rubella case, whose nucleotide sequence matched a strain found in China (RVi/Tianjin.CHN/46.18/1), acquired their infection whilst in Hong Kong SAR, China.

There were no notifications of rubella CRS cases to the Australian Department of Health in 2018.

Table 3 provides a de-identified line-listing of rubella genotyping data by state and territory, virus lineage and WH0 representative strain.

Figure 1: Distribution of wild-type measles genotype identified at VIDRL epi-week, January to December 2018.

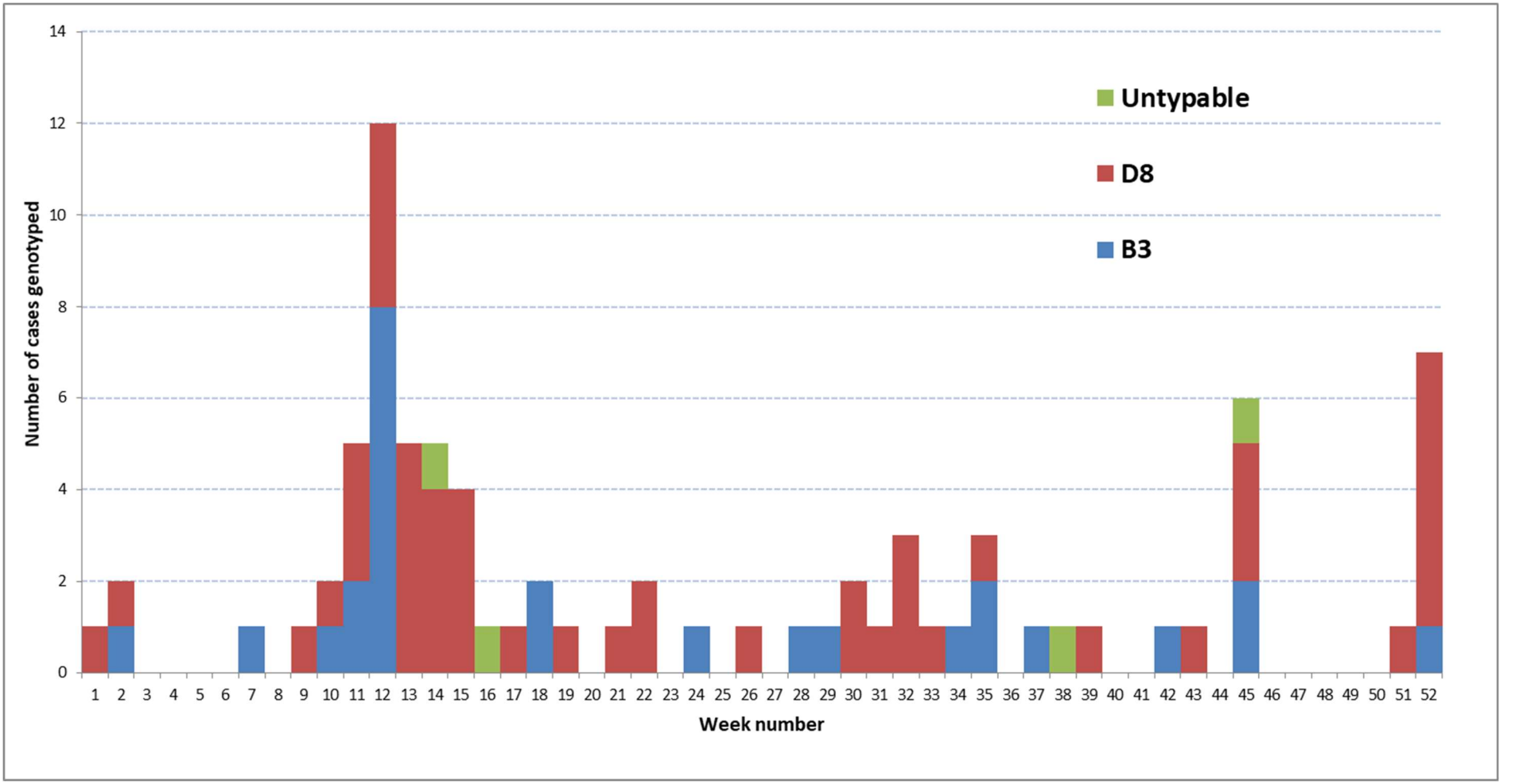
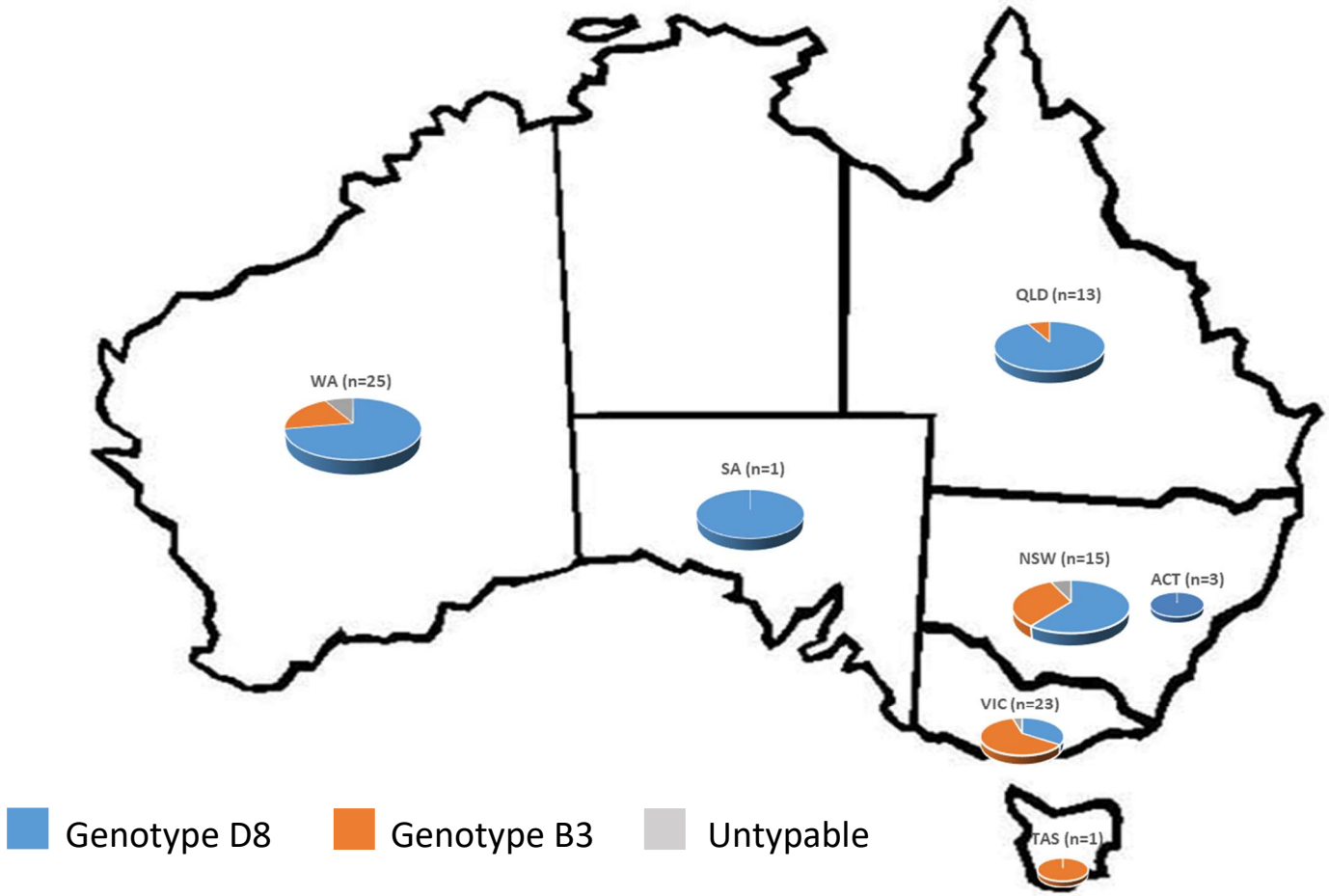


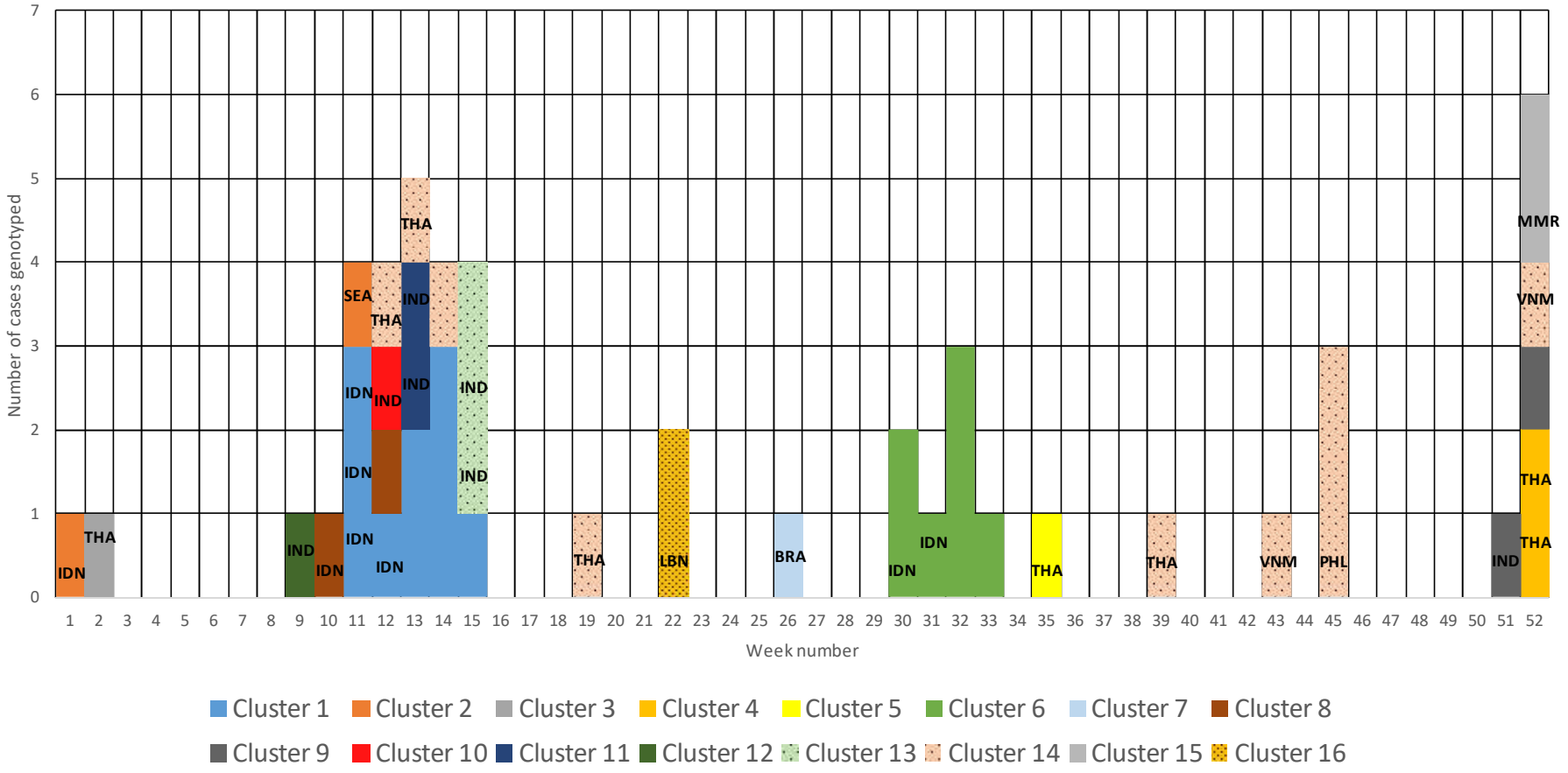
Figure 2: Geographical distribution of measles genotypes in Australia, 2018



Note: size of pie charts not proportional to the number of cases genotypes.

Figure 3: Distribution of measles genotype D8 cases by epi-week, January to December 2018.

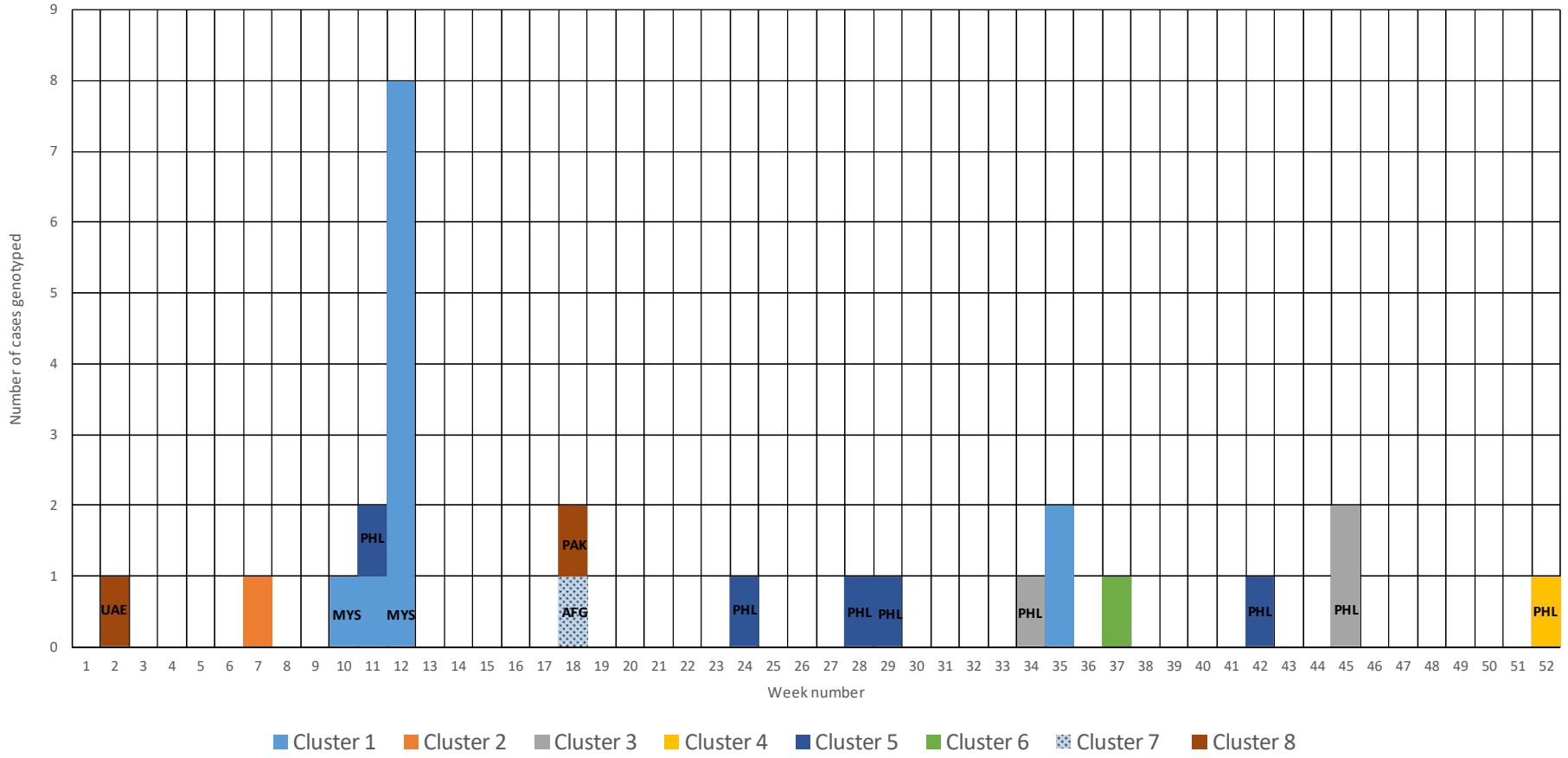
Clusters determined by Figure 5 phylogeny.



Country/region codes of importation associated with measles index cases are indicated (BRA=Brazil; IDN=Indonesia; IND=India; LBN=Lebanon; MMR=Myanmar; PHL=Philippines; SEA= South East Asia; THA=Thailand; VNM=Vietnam)

Figure 4: Distribution of measles genotype B3 cases by epi-week, January to December 2018.

Clusters determined by Figure 6 phylogeny.



Country codes of importation associated with measles index cases are indicated (AFG=Afghanistan; MYS=Malaysia; PAK=Pakistan; PHL=Philippines; UAE=United Arab Emirates)

Figure 5: N450 phylogenetic relationships among measles genotype D8 strains identified in Australia, 2018.

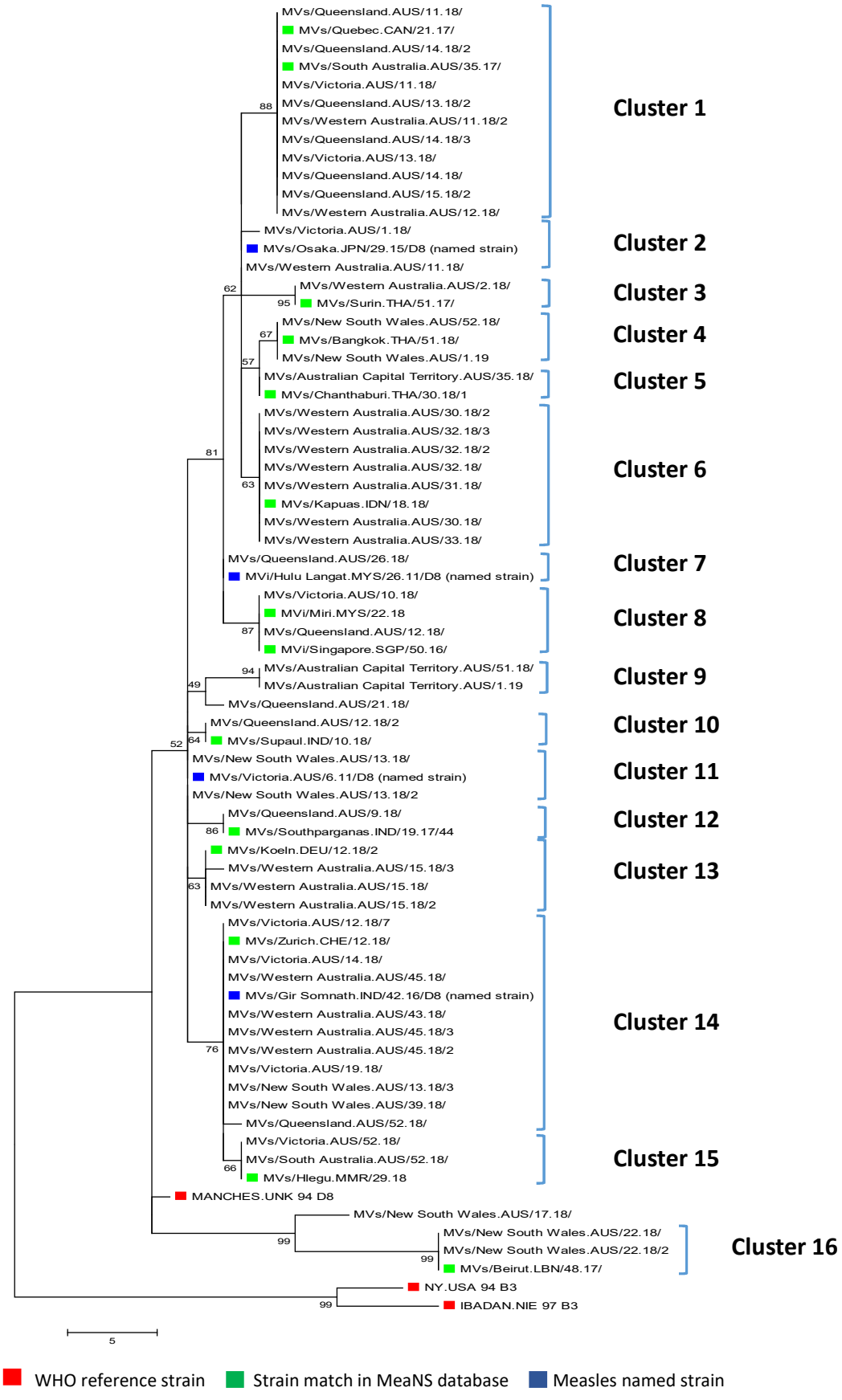


Figure 6: N450 phylogenetic relationships among measles genotype B3 strains identified in Australia, 2018.

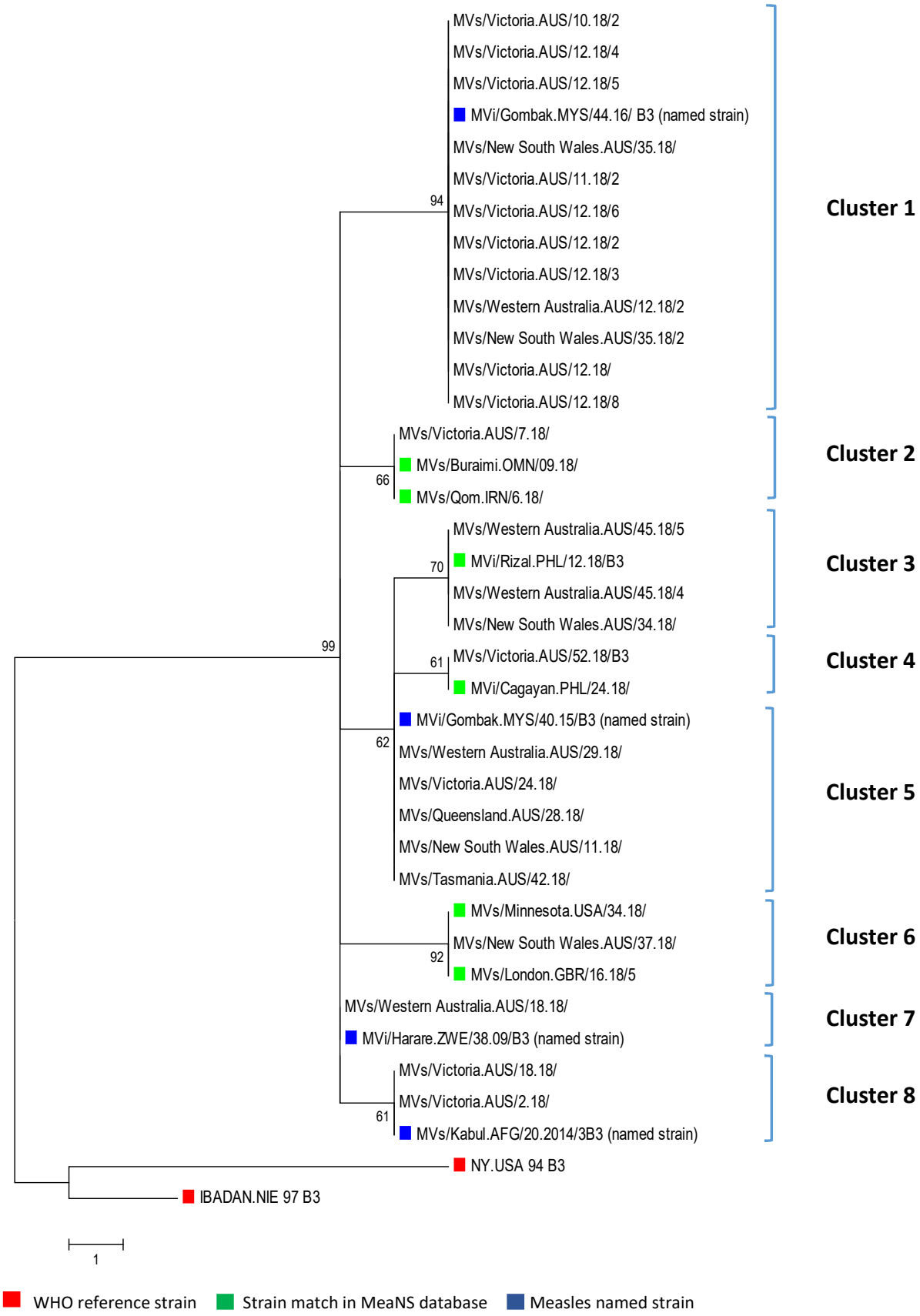
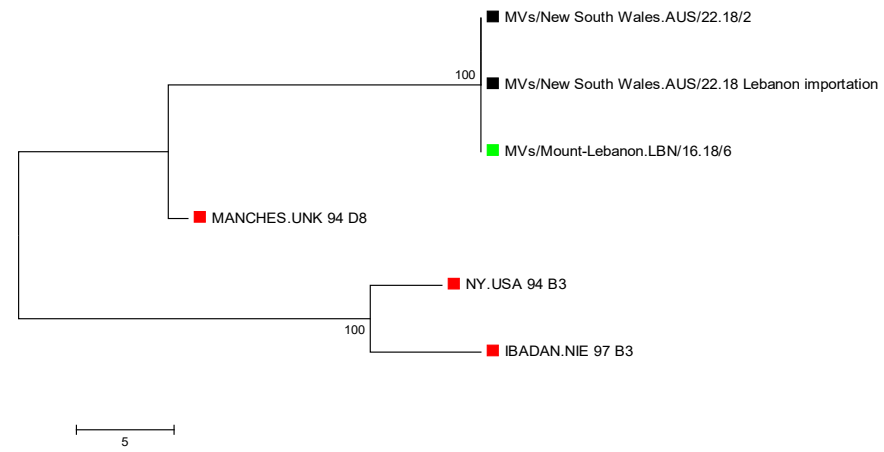


Figure 7A: N450 phylogenetic relationship among cases of NSW outbreak 1

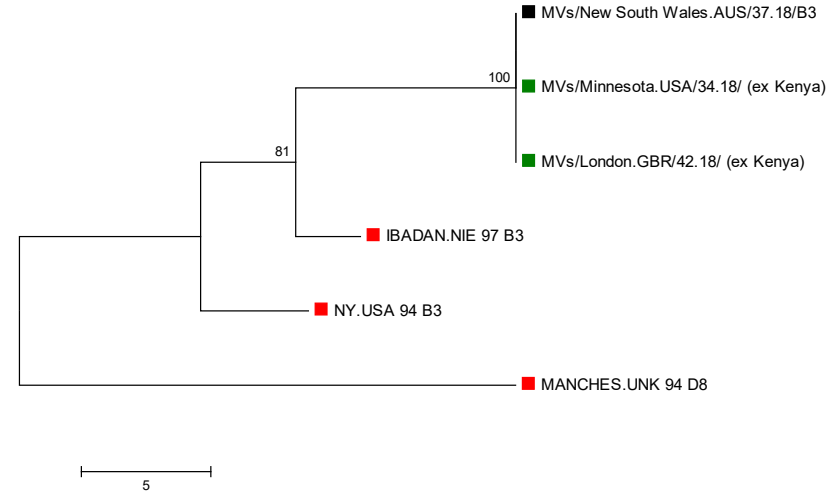


Outbreak cases

WHO reference strain

Strain match in MeaNS database

Figure 7B. N450 phylogenetic relationship among cases of NSW outbreak 2



Outbreak cases

WHO reference strain

Strain match in MeaNS database

Figure 7C: N450 phylogenetic relationship among cases of VIC outbreak 1

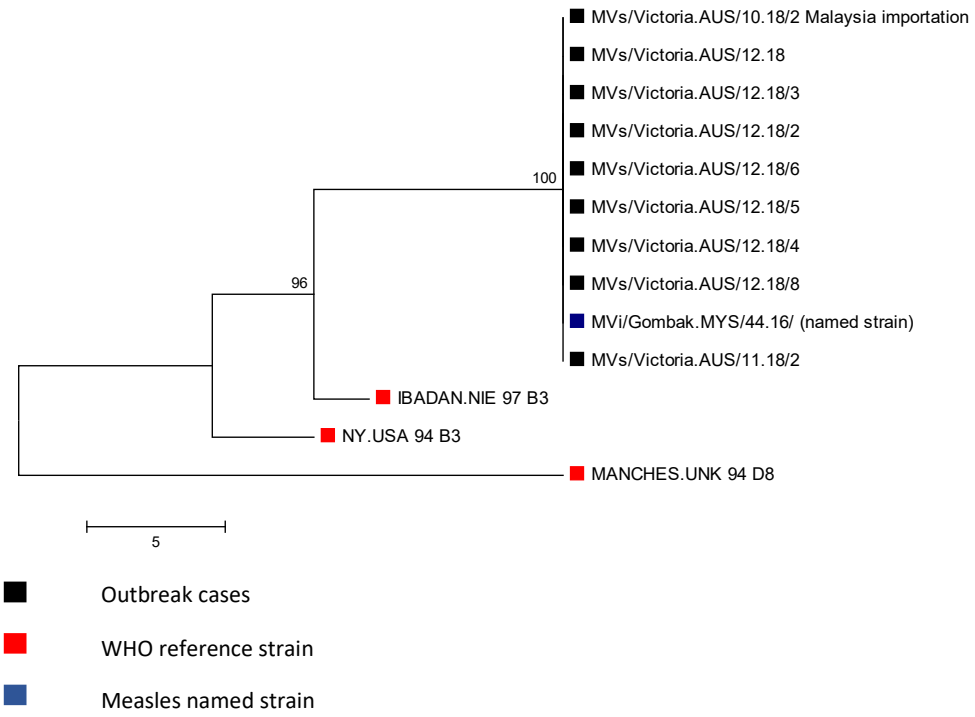


Figure 7D. N450 phylogenetic relationship among cases of VIC outbreak 2

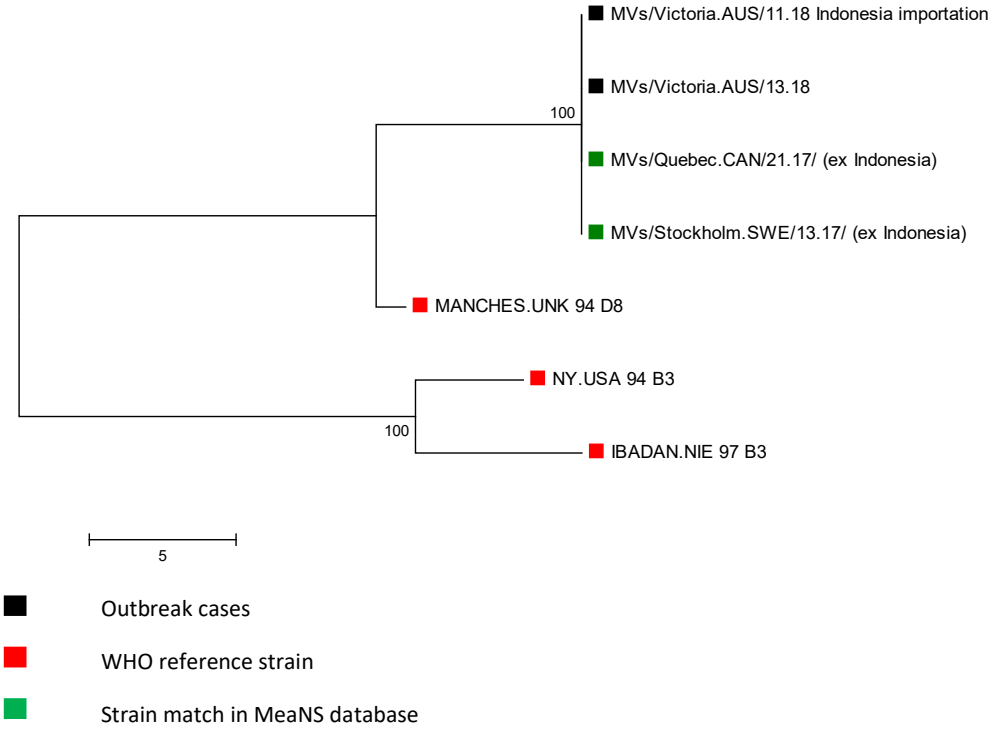
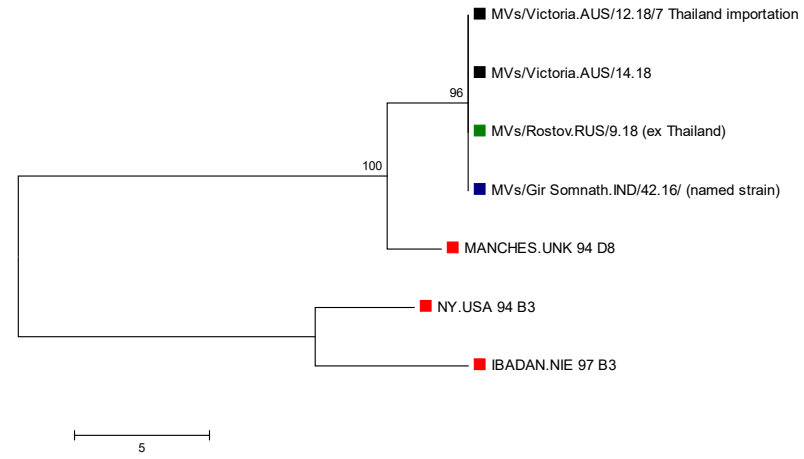


Figure 7E: N450 phylogenetic relationship among cases of VIC outbreak 4



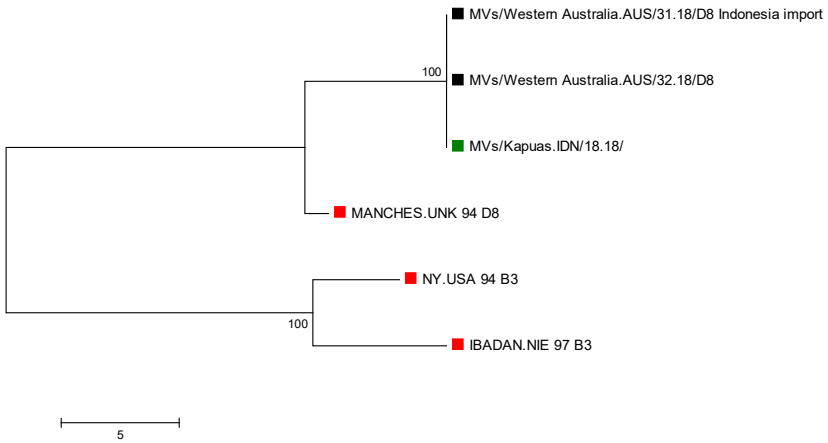
Outbreak cases

WHO reference strain

Strain match in MeaNS database

Measles named strain

Figure 7F. N450 phylogenetic relationship among cases of WA outbreak 1

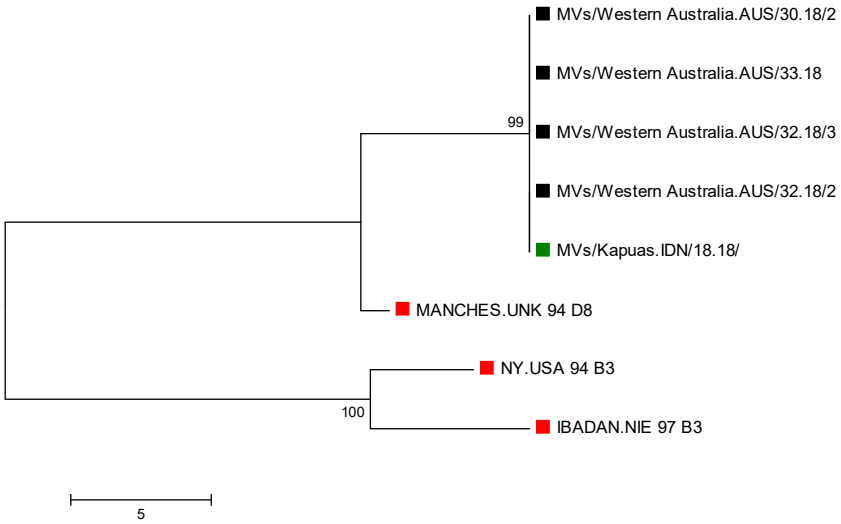


Outbreak cases

WHO reference strain

Strain match in MeaNS database

Figure 7G: N450 phylogenetic relationship among cases of WA outbreak 2

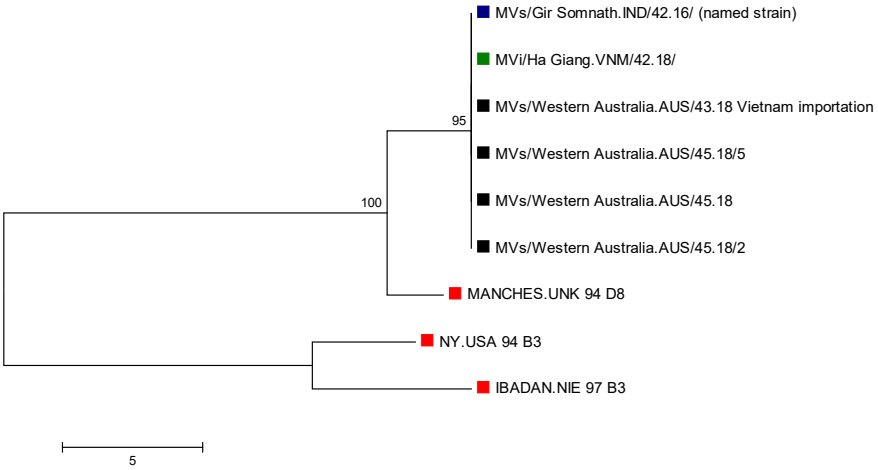


Outbreak cases

WHO reference strain

Strain match in MeaNS database

Figure 7H. N450 phylogenetic relationship among cases of WA outbreak 3



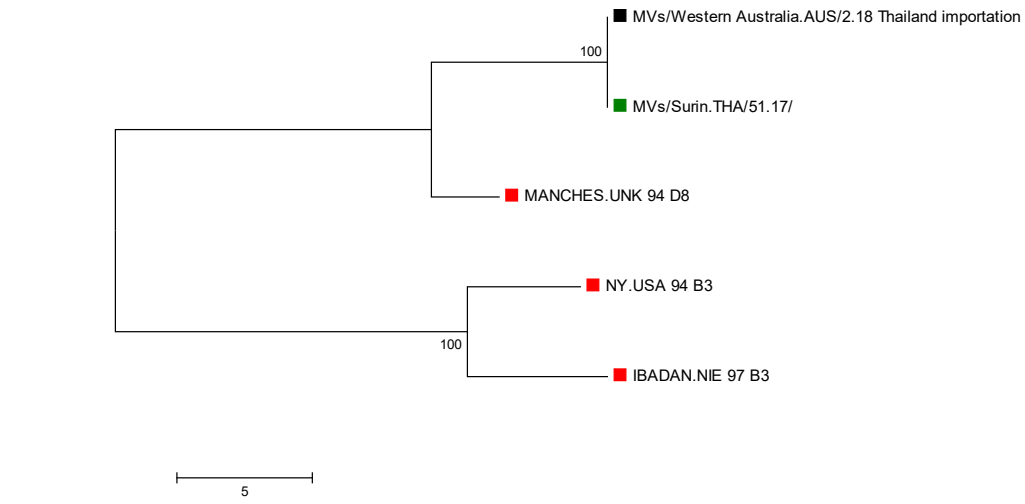
Outbreak cases

WHO reference strain

Strain match in MeaNS database

Measles named strain

Figure 7I: N450 phylogenetic relationship among cases of WA outbreak 5

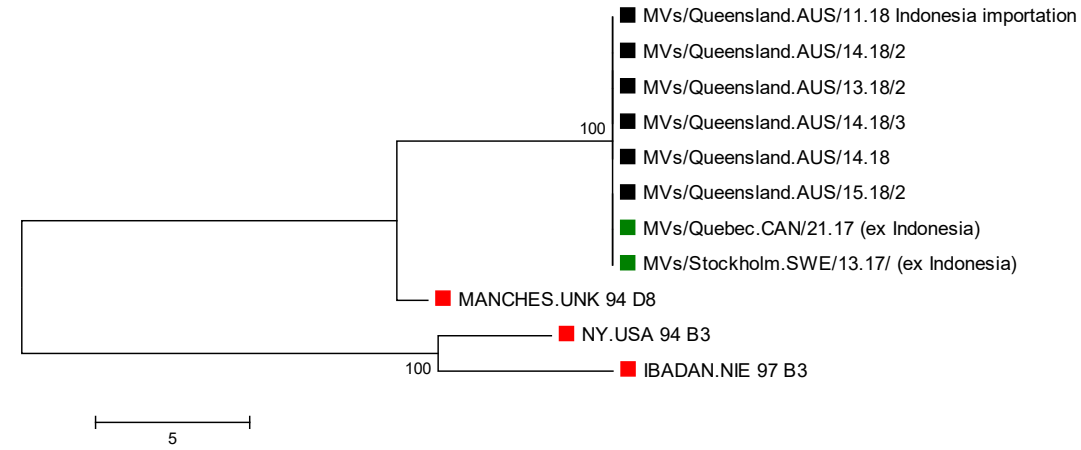


Outbreak cases

WHO reference strain

Strain match in MeaNS database

Figure 7J. N450 phylogenetic relationship among cases of QLD outbreak 1



Outbreak cases

WHO reference strain

Strain match in MeaNS database

Figure 8: Rubella E1-739 phylogenetic relationship among rubella strains identified in Australia, 2018.