# Flavivirus infection

## Australian national notifiable diseases case definition

This document contains the surveillance case definition for flavivirus infection, which is nationally notifiable within Australia. State and territory health departments use this definition to decide whether to notify the Australian Government Department of Health and Aged Care of a case.

| Version | Status | Last reviewed | Implementation date |
|---|---|---|---|
| 1.0 | Initial CDNA case definition | 2004 | 2004 |

### Note

1. It is recognised that some cases of human infection cannot be attributed to a single flavivirus. This may either be because the serology shows specific antibody to more than one virus, specific antibody cannot be assigned based on the tests available in Australian reference laboratories, or a flavivirus is detected that cannot be identified.
2. Confirmation by a second arbovirus reference laboratory is required if the case cannot be attributed to known flaviviruses.
3. Occasional human infections occur due to other known flaviviruses, such as Kokobera, Alfuy, Edge Hill and Stratford viruses.

### Reporting

Only **confirmed cases** should be notified.

### Confirmed case

A confirmed case requires **laboratory definitive evidence** AND **clinical evidence.**

#### Laboratory definitive evidence

1. Isolation of a flavivirus that cannot be identified in Australian reference laboratories or which is identified as one of the flaviviruses not otherwise classified

OR

2. Detection of a flavivirus, by nucleic acid testing, that cannot be identified in Australian reference laboratories or which is identified as one of the flaviviruses not otherwise classified

OR

3. IgG seroconversion or a significant increase in antibody level or a fourfold or greater rise in titre of flavivirus specific IgG that cannot be identified or which is identified as being specific for one of the flaviviruses not otherwise classified. There must be no history of recent Japanese encephalitis or yellow fever vaccination

OR

4. Detection of flavivirus IgM in cerebrospinal fluid, with reactivity to more than one flavivirus antigen (Murray Valley encephalitis, Kunjin, Japanese Encephalitis and/or dengue) or with reactivity only to one or more of the flaviviruses not otherwise classified

OR

5. Detection of flavivirus IgM in the serum, with reactivity to more than one flavivirus antigen (Murray Valley encephalitis, Kunjin, Japanese Encephalitis and/or dengue) or with reactivity only to one or more of the flaviviruses not otherwise classified. This is only accepted as laboratory evidence for encephalitic illnesses. There must be no history of recent Japanese encephalitis or yellow fever vaccination

Clinical evidence

1. Non-encephalitic disease: acute febrile illness with headache, myalgia and/or rash

OR

2. Encephalitic disease: acute febrile meningoencephalitis characterised by one or more of the following:

- focal neurological disease or clearly impaired level of consciousness
- an abnormal computerised tomograph or magnetic resonance image or electrocardiograph
- presence of pleocytosis in cerebrospinal fluid.

# Australian national notifiable diseases case definitions - Zika virus case definition

Confirmed and probable cases are nationally notifiable under the disease *Flavivirus infection (unspecified)* using the Organism Name field to specify infection with Zika virus (ZIKV).

## Reporting

Both **confirmed** and **probable** cases are nationally notifiable. Both confirmed and probable cases should be further sub-classified into clinical and non-clinical cases.

### Confirmed case

A confirmed case requires **laboratory definitive evidence** only. Clinical evidence should be used to sub-classify cases as clinical or non-clinical.

#### Laboratory definitive evidence

- Detection of ZIKV by nucleic acid testing or virus isolation;

OR

- IgG seroconversion or a significant increase in antibody level or a fourfold or greater rise in titre of ZIKV-specific IgG, and recent infection by dengue or other epidemiologically possible flaviviruses has been excluded;

OR

- Detection of ZIKV-specific IgM in cerebrospinal fluid, in the absence of IgM to other possible infecting flaviviruses.

### Probable case

A probable case requires **laboratory suggestive evidence** AND **epidemiological evidence**. Clinical evidence should be used to sub-classify cases as clinical or non-clinical.

#### Laboratory suggestive evidence

Detection of ZIKV-specific IgM in the absence of IgM to other epidemiologically possible flaviruses or flavivirus vaccination in the 3 weeks prior to testing.

Notes:

- If the date of most recent exposure was greater than 4 weeks before the specimen date, then ZIKV-specific IgG must also be positive.
- If ZIKV-specific IgG was initially negative and subsequent testing greater than 4 weeks after exposure fails to demonstrate seroconversion the case should be rejected.

### Epidemiological evidence

#### Clinical case

- Travel to or residence in a ZIKV receptive country[1] or area in Australia within two weeks prior to symptom onset;

OR

- Sexual exposure to a confirmed or probable case of ZIKV infection within two weeks prior to symptom onset.

#### Non-clinical case

- Travel to or residence in a ZIKV receptive country[1] or area in Australia within two months prior to specimen date.

OR

- Sexual exposure to a confirmed or probable case of ZIKV infection within two months prior to specimen date.

## Clinical case

Both confirmed and probable cases should be further sub-classified into **clinical** or **non-clinical** cases.

### Clinical evidence

An acute illness within 2 weeks of exposure with 2 or more of the following symptoms:

- Fever
- Headache
- Myalgia
- Arthralgia
- Rash
- Non-purulent conjunctivitis.

In the absence of clinical evidence, the case will be classified as non-clinical.

# Australian national notifiable diseases case definitions - congenital Zika virus infection case definition

Confirmed and probable cases are nationally notifiable under the disease *Flavivirus infection (unspecified)* using the Organism Name field to specify congenital ZIKV infection.

## Reporting

Both **confirmed** and **probable** cases are nationally notifiable.

### Confirmed Case

A confirmed case requires **laboratory definitive evidence** only.

#### Laboratory definitive evidence

Fetal (at 20 weeks gestation or more)

Isolation or detection of ZIKV from appropriate clinical samples (i.e. fetal blood, amniotic fluid, chorionic villus sample or post-mortem cerebrospinal fluid or tissue) by viral culture or nucleic acid testing.

Infant (within 28 days following birth)

Isolation or detection of ZIKV from appropriate clinical samples by viral culture or nucleic acid testing, with no history of travel since birth to, or residence in, a ZIKV receptive country[1] or area in Australia.

### Probable Case

A probable case requires clinical evidence AND epidemiological evidence.

#### Clinical evidence

Microcephaly[2,3,4,5,6] or other CNS abnormalities[7] in the infant or fetus (in the absence of any other known cause).

#### Epidemiological evidence

Confirmed or probable ZIKV infection in the mother during pregnancy.

# Footnotes

1. ZIKV receptive countries and areas are outlined on the Global Consensus Map at http://www.healthmap.org/dengue/en/. Areas are considered receptive to ZIKV where the likelihood of local acquisition is placed on the map as 'uncertain' or more.
2. Head circumference <-2SD below mean for gestation.
3. WHO Assessment of infants with microcephaly in the context of ZIKV. Interim guidance. 4 March 2016, WHO/ZIKV/MOC/16.3 Rev.1.
4. WHO Growth standards for term neonates (http://www.who.int/childgrowth/standards/en/)
5. WHO Pregnancy management in the context of ZIKV. Interim guidance. 2 March 2016. WHO/ZIKV/MOC/16.2
6. Intergrowth standards for preterm neonates (Villar, José et al. (2014). International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. Lancet; (384). 9946: 857–868)
7. These include: ventriculomegaly, calcifications, abnormal sulcation and gyration, brain atrophy, callosal dysgenesis, microophthalmia, eye calcifications.