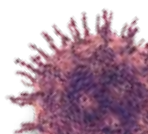


Establishing syndromic surveillance and  
event-based surveillance systems for  
**Zika, dengue** and other  
**arboviral diseases**



World Health  
Organization

REGIONAL OFFICE FOR THE Eastern Mediterranean





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# Contents

1. Introduction.....	7
2. Scope of this publication .....	7
3. Rationale for this publication .....	8
4. Main objective.....	9
5. The organisms and the diseases .....	9
6. The syndromic surveillance approach in the Eastern Mediterranean Region.....	10
7. Early detection: is it dengue, chikungunya, yellow fever, Zika or another disease? .....	11
7.1 Case definitions (suspected, confirmed) .....	11
7.2 Early detection of cases using the syndromic surveillance approach.....	12
8. Implementing a surveillance system for early detection .....	14
9. Event-based surveillance for arboviral diseases .....	15
9.1 Definition of event-based surveillance .....	16
9.2 Minimum requirements of event-based surveillance .....	16
9.3 Sources of information .....	16
9.4 Examples of events captured by event-based surveillance for arboviral infection and the verification process.....	17
9.5 Methods of reporting from the sources of information.....	18
9.6 Specific surveillance strategy for early recognition of complications of Zika virus infection.....	18
10. How vector surveillance can help in early detection.....	19
11. Laboratory role and services .....	20
12. Integration of syndromic surveillance and event-based surveillance .....	22
13. Main challenges for implementation .....	22
14. Strategic requirements to implement/strengthen the system .....	23
15. Practical requirements for running the system .....	23
16. Monitoring and evaluation of the system .....	25
Bibliography .....	26
Annexes.....	27
Annex 1. <i>Main epidemiological and clinical characteristics of Zika virus,         dengue and chikungunya</i> .....	27
Annex 2. <i>Classification of case definitions of Zika, dengue and chikungunya</i> .....	33
Annex 3. <i>Examples of surveillance and control measures for Aedes mosquitoes</i> .....	34
Annex 4. <i>Algorithm for data flow for a syndromic surveillance system         in the event of any of the arboviral diseases being detected</i> .....	35
Annex 5. <i>Algorithm for arbovirus detection for suspected cases of dengue,         Zika or chikungunya</i> .....	36

<b>Annex 6.</b> <i>Suggested process for using the acute flaccid paralysis (AFP) surveillance system for Zika virus surveillance.....</i>	<b>37</b>
<b>Annex 7.</b> <i>Potential sources of information and means of collection .....</i>	<b>38</b>
<b>Annex 8.</b> <i>Examples of event investigation and data collection forms .....</i>	<b>40</b>
<b>Annex 9.</b> <i>Operational priorities for entomological surveillance in the context of Zika virus .....</i>	<b>43</b>

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## 1. Introduction

In view of the threat of Zika and other emerging arboviral diseases with epidemic potential, there is an urgent need to develop better systems for early detection of and response to these high threat diseases in the Eastern Mediterranean Region of the World Health Organization (WHO). The Infectious Hazard Management unit in WHO's Health Emergencies Programme, through consultations with countries and lead experts in the Region, therefore developed this strategic framework for establishing syndromic and event-based surveillance systems for Zika, dengue and other arboviral diseases.

On 1 February 2016, WHO declared a public health emergency of international concern with regard to clusters of microcephaly and neurological disorders potentially associated with Zika virus.<sup>1</sup> This called for scaling up preparedness and readiness for mitigating the threat of Zika virus infection and other arboviral diseases transmitted by *Aedes* mosquitoes.

The *Aedes* mosquitoes that transmit arboviruses, including Zika virus, are present in several countries in the Eastern Mediterranean Region, and a number of countries have reported repeated outbreaks of dengue, chikungunya and yellow fever. Thus, there is an urgent need to develop capacity for early detection and response to Zika and other arboviral disease outbreaks in the Region.

Following emergency regional meetings that were conducted in February 2016 to enhance preparedness for Zika and other arboviral diseases, countries of the Region identified several important gaps, one of which was inadequate disease surveillance for efficient action.<sup>2</sup> One of the key priority activities identified was the establishment of effective surveillance systems for Zika and other arboviral diseases to improve regional capacity for surveillance, risk assessment and epidemiological investigation around suspected or confirmed cases of Zika, dengue, chikungunya and yellow fever. This framework aims to help countries to enhance the early detection of Zika virus infection and other arboviral diseases based on the syndromic surveillance and event-based surveillance approaches.

## 2. Scope of this publication

This publication aims to provide the key components for the implementation of syndromic surveillance and event-based surveillance for early detection of clusters of Zika virus and other arboviral diseases (dengue, chikungunya and yellow fever) transmitted by *Aedes* mosquitoes.

It should be considered as a tool to strengthen the current surveillance system rather than replace the existing system altogether.

<sup>1</sup> WHO statement on the first meeting of the International Health Regulations (2005) (IHR 2005) Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations. Geneva: World Health Organization; 2016.

<sup>2</sup> Extracted from the Summary report on the Regional meeting to enhance preparedness and response capacities to Zika virus infection, Cairo, Egypt 22–23 February 2016; and Casablanca, Morocco 28–29 February 2016. Cairo: WHO Regional Office for the Eastern Mediterranean; 2016:WHO-EM/CSR/099/E.

Later in this publication event-based surveillance will be explained in detail so that countries may develop manuals of their own which suit their individual settings and circumstances. Whenever details are mentioned it is for the purpose of demonstration rather than prescribing the future capabilities and interests of countries as they develop their own guidelines and procedures. Furthermore, this publication focuses mainly on Zika and other arboviral diseases (dengue, chikungunya and yellow fever) and proposes key guidance for integration in the process of surveillance: no details are provided for setting up surveillance of the main complications of Zika virus (Guillain-Barré syndrome and microcephaly). It is beyond the scope of this publication to predict the response required by health systems when an event is detected in relation to arboviruses. However, it is worth briefly mentioning the important role and expected impact of event-based surveillance/syndromic surveillance on the efficiency of the required responses, and the early detection of disease.

The information in this publication is based on the most relevant available evidence and is subject to modifications and updates in light of new information that may emerge.

### 3. Rationale for this publication

Reasons for applying a syndromic surveillance system and event-based surveillance for Zika and related arboviral diseases:

- early detection of outbreaks and illness clusters related to these diseases; and
- to increase the sensitivity, rather than specificity, of the surveillance system to early identify disease and to use existing health data in real time to provide immediate analysis, investigation feedback and follow-up of potential outbreaks.

**The advantages are:**

- easy implementation of syndromic and event-based surveillance systems within the conventional system;
- syndromic definitions for large-scale early detection and monitoring of outbreaks have been identified;
- enhancing collaboration between public health agencies, health care professionals, community, industry, etc.;
- easy to be piloted, tested and implemented and then modified;
- easy to measure effectiveness and follow up on implementation;
- can capture other events, even those not related to arboviruses;
- cost-effectiveness;
- can be a good start towards developing more comprehensive event-based surveillance for other diseases and events;
- provides reasonable information for early response;
- will work at community level;
- if implemented, will satisfy a major International Health Regulation (IHR) (2005) requirement;
- can be used in areas with restricted/limited access, e.g. due to conflict; and
- the same reporting persons at the community level can play an important role in providing contingency measures for local communities, thus improving response.

**The disadvantages are:**

- need to dedicate human and other resources for data management and analysis;
- optimal syndrome definitions for continuous monitoring and specific data sources for Zika and other arboviral diseases have not yet been properly identified;
- needs a clear definition of country gap analysis and risk assessment up to the locality level so as to support the standard/routine conventional surveillance system; and
- if implemented at the community level, the cost of collecting and communicating data may be substantial (mobile phones, register books, transportation fees) and proper training and incentives for commitment will be required.

**4. Main objective**

The main objective of this publication is to define an affordable surveillance strategy for early detection of clusters of Zika virus and other arboviral diseases using the syndromic surveillance and event-based surveillance approaches.

**5. The organisms and the diseases**

Dengue, chikungunya, yellow fever and Zika viruses are most commonly transmitted by *Aedes* mosquitoes.

Dengue virus is a single-stranded RNA virus of the family Flaviviridae, genus *Flavivirus*, with four serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Chikungunya is a single-stranded RNA virus that belongs to the family Togaviridae, genus *Alphavirus*. Zika virus is a single-stranded RNA virus of the family Flaviviridae, genus *Flavivirus*. The main epidemiological and clinical characteristics of Zika virus, dengue and chikungunya are presented in detail in Annex 1.

Anyone who lives in or has travelled to an area where dengue, chikungunya or Zika viruses are found is at risk of infection.

**Key messages about Zika virus**

- Consider testing for Zika virus infection if there has been a compatible illness, i.e. syndromes of prolonged fever and/or maculopapular rash plus conjunctivitis with onset of symptoms, within two weeks of returning from an area with active Zika virus transmission.
- Pregnant women who become infected with the Zika virus can transmit the disease to their unborn babies.
- Advise pregnant women and women trying to get pregnant to consider postponing travel to any country with active Zika virus transmission.
- Refer pregnant women who have travelled to a country with active Zika virus transmission and who have had relevant symptoms to their general practitioner or obstetrician for advice and counselling.
- Advise travellers to follow recommendations for avoiding mosquito bites when travelling in countries and areas where there is a risk of any mosquito-borne disease.

**KEY ELEMENT 1.**

This publication outlines a strategic regional framework to enhance syndromic surveillance for arboviral diseases transmitted by *Aedes* mosquitoes (dengue, chikungunya, yellow fever, Zika) but it is often necessary to contextualize according to a country's needs and capacities.

**KEY ELEMENT 2.**

Countries should take the opportunity to better integrate syndromic surveillance/event-based surveillance within their existing systems for the early warning component in the context of IHR (2005) requirements and obligations.

## 6. The syndromic surveillance approach in the Eastern Mediterranean Region

**KEY ELEMENT 3.**

Syndromic surveillance is defined as a method of surveillance that uses health-related data based on clinical observations rather than laboratory confirmation of diagnoses.<sup>1</sup> Syndromic surveillance is used to detect outbreaks earlier than would otherwise be possible with methods based on laboratory diagnosis. Case definitions used for syndromic surveillance are based on clinical signs and symptoms rather than on specific laboratory criteria for confirmation of the causative agent.

Syndromic surveillance, using routinely available data on health and non health-related issues, is now being used in many countries, especially in the European and Western Pacific regions. It is used for early detection of outbreaks and clusters of health events with the aim of rapidly responding to them. It is based on timely collection, collation, analysis, interpretation and dissemination of prediagnostic data from different sources to enhance detection of outbreaks and reduce the mortality, morbidity and economic impact of such outbreaks.

In 2011 the Islamic Republic of Iran became the first country in the Eastern Mediterranean Region to examine the possibility of instigating a syndromic surveillance system and completed a pilot phase in June 2017. Some other countries in the Region have since moved to do so, including Lebanon, Morocco and Tunisia.

<sup>1</sup> Communicable disease alert and response for mass gatherings: key considerations. Geneva: World Health Organization; 2008.

## 7. Early detection: is it dengue, chikungunya, yellow fever, Zika or another disease?

### KEY ELEMENT 4.

Certain steps should be followed to establish which arboviral disease is present in the country.

- Critical risk assessment should be carried out based on geographic, demographic and other risk factors for dengue, chikungunya, yellow fever and Zika virus infections and the level of risk for the country in the context of these diseases assessed.
- Critical evaluation of data flow capabilities and analysis should be established.
- An early detection system should be implemented within the existing surveillance system: include syndromic surveillance and event-based surveillance based on case definitions.
- Clear mapping and defining of laboratory capabilities should be developed and a clear referral pathway for laboratory (reference centre) confirmation of the sample validated.

### 7.1 Case definitions (suspected, confirmed)

Taking into account the main existing case definitions, comparisons and classifications related to these diseases (Table 1) and other case definitions (Annex 2), the syndromic case definition for arboviral diseases could be fever AND at least one of the following symptoms: myalgia/arthralgia, maculopapular rash, retro-orbital pain, conjunctivitis, headache, vomiting or jaundice.

### KEY ELEMENT 5.

Significant sensitivity is required to increase the level of detection, alongside significant specificity to detect what should be detected. The syndromic surveillance system needs to be set up to capture a wide range of potential cases and be specific enough to filter those cases.

### KEY ELEMENT 6.

Some difficulties may be encountered at country level in the adaptation and standardization processes for case definitions used for the syndromic surveillance approach.

- Allocate resources from policy-makers to validate syndromic case definitions.
- Ensure collaboration with clinical medicine such as hospitals and private clinics to report complications (Guillain-Barré syndrome, microcephaly, etc.).
- Ensure timely reporting, a key element in syndromic surveillance.
- Case definition should be applied only during specific high-risk situations or seasons.
- Responsiveness of system is crucial (immediate detection and response).

**Table 1.** Classification of case definitions of dengue, chikungunya, yellow fever and Zika

Symptom	Dengue	Chikungunya	Yellow fever	Zika
Fever	++++	+++	+++	+++
Myalgia/arthralgia	+++	++++	++	++
Maculopapular rash	++	++	+	+++
Conjunctivitis	0	+	0	+++
Retro-orbital pain	++	+	0	++
Headache	++	++	++	++
Vomiting	++	++	++	++
Jaundice	0	0	+++	0
Lymphadenopathies	++	++		+
Hepatomegaly	0	+++	0	0
Oedema of extremities	0	0	0	++
Haemorrhage (petechiae, ecchymosis, purpura, epistaxis, bleeding gums, haematuria, or a positive tourniquet test result)	+	0	++	0
Oropharynx and facial erythema	+	0	0	0

Note: symbols above refer to the frequency or likelihood of a symptom being present among cases: ++++ = typically present; +++ = often present; ++ = sometimes present; + = seldom present.

#### KEY ELEMENT 7.

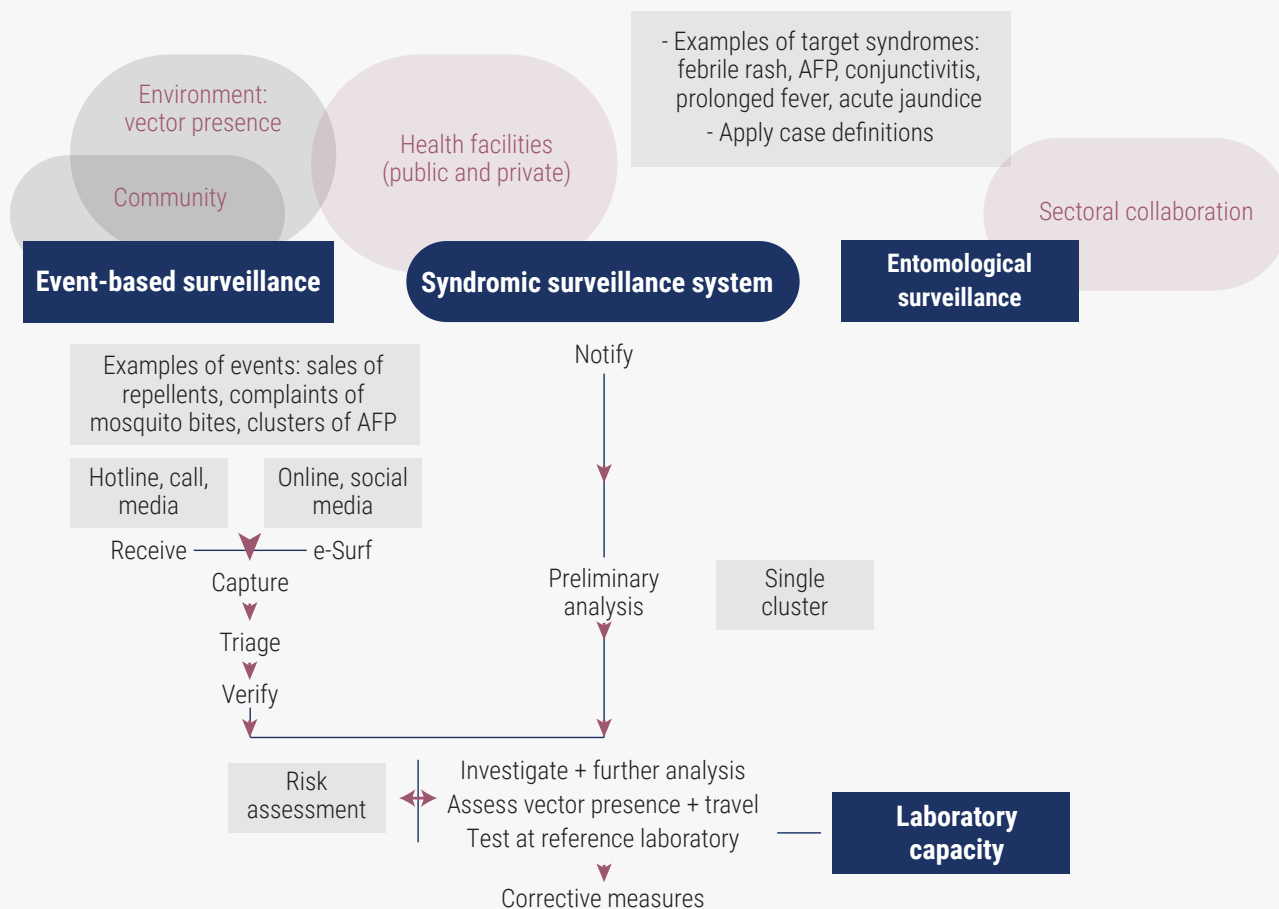
For Zika virus disease, any observation of Guillain-Barré syndrome or neurological malformations such as microcephaly at birth by clinicians in health facilities could be a warning signal to be verified.

## 7.2 Early detection of cases using the syndromic surveillance approach

The rationale for using the syndromic surveillance approach for arboviral diseases transmitted by *Aedes* mosquitoes (Zika, chikungunya and dengue) is to bring suspected cases to the attention of the health system early, before clinical or laboratory confirmation, as shown in Fig. 1.

In the process of preliminary analysis, syndromic surveillance takes into account the differential diagnosis of other diseases that have a similar clinical picture, as shown in Table 2.

For example, the diagnosis of dengue is typically made clinically on the basis of reported symptoms and physical examination; this applies especially in endemic areas. However, early disease can be difficult to differentiate from other viral infections based on syndromes of prolonged fever or maculopapular rash (Table 2). A probable diagnosis is based on the findings of fever plus two of the following: nausea and vomiting, rash, generalized pains, low white blood cell count, positive tourniquet test and third space fluid accumulation by ultrasonography (pericardial effusion, pleural effusion, ascites), or any warning sign (see Annex 2). Warning signs require hospital-specific monitoring.



**Fig. 1.** Algorithm for the process of early detection for the syndromic surveillance system and event-based surveillance

**Table 2.** Differential diagnosis of arboviral diseases

Dengue	Chikungunya	Yellow fever	Zika
Zika, chikungunya, influenza, malaria, West Nile fever, yellow fever, Japanese encephalitis	Dengue, Zika, malaria, leptospirosis, parvovirus, enterovirus, group A streptococcus, rubella, measles, adenovirus, post-infectious arthritis, rheumatologic conditions, alphavirus infections	Viral hepatitis, malaria, dengue, typhoid fever, leptospirosis, Ebola disease, Lassa fever	Dengue, chikungunya malaria, rubella, measles, parvovirus, adenovirus, enterovirus, leptospirosis, rickettsiosis, group A streptococcus

Source: adapted from Tool for the diagnosis and care of patients with suspected arboviral diseases. Washington (DC): Pan American Health Organization; 2017 (<http://iris.paho.org/xmlui/handle/123456789/33895>).

It can be difficult to distinguish chikungunya from dengue, a similar viral infection that shares many symptoms (especially prolonged fever and maculopapular rash), and which occurs in the same parts of the world. Often, investigations are performed so as to exclude other conditions that cause similar symptoms such as malaria, leptospirosis, viral haemorrhagic fever, typhoid fever, meningococcal disease, measles and influenza. Zika also has symptoms similar to those of dengue.

In the context of the syndromic surveillance approach, warning signs are an important aspect of early detection of potentially serious disease, while the evidence for any specific clinical or laboratory markers is weak or not available.

#### KEY ELEMENT 8.

In areas where the *Aedes* mosquito is present, syndromic surveillance should be especially enhanced during the mosquito breeding season.

Syndromic surveillance should be based mainly on the case definition and the occurrence of clusters. (Cluster definition: two or more cases with plausible epidemiological links in terms of time, place and relationship.)

When syndromic surveillance has been enhanced at all levels, starting with primary health care, health workers should then report the number of cases corresponding to the case definition and whether clusters are of the same syndrome. After receiving a verified indication of a cluster of cases of the targeted syndrome, the investigation should start at district level by completing the epidemiological sheet and collecting samples for laboratory confirmation. At this level random samples can be taken.

In district/regional hospitals, if warning signs (selected syndromes or complications such as clusters of Guillain-Barré syndrome or microcephaly) (Annex 2) related to *Aedes*-borne diseases are reported, samples should be collected and transferred to the reference laboratory. A well-established referral pathway and clear guidance for the process of early detection should be in place. An example of a syndromic surveillance algorithm for arboviral diseases is presented in Annex 4.

During epidemiological investigation of suspected clusters of syndromes, cases with the same syndromes are further assessed. Samples should be collected from febrile patients within five days of onset of illness and sent for serological and polymerase chain reaction (PCR) testing. An algorithm for laboratory tests is shown in Annex 5.

In addition, practical mechanisms for collaboration between entomological and epidemiological surveillance should be in place. Active surveillance for circulating vectors should be conducted in and around areas where a case of dengue, chikungunya, yellow fever or Zika has been confirmed.

## 8. Implementing a surveillance system for early detection

It is difficult for any existing surveillance system to detect all cases. Imported cases are often overlooked: travellers do not always seek medical care locally, and some people go to private practitioners who are less likely to report cases. A very sensitive syndromic surveillance system is needed to detect cases in countries where indigenous transmission is low or absent. Such a system requires that the quality of surveillance be regularly monitored and validated. The different conditions required to permit early detection in different situations need to be specified as part of the system.



There are some examples among existing surveillance systems, e.g. polio surveillance systems, that could be used for the detection of Zika virus infection. Existing national polio surveillance systems collectively present a platform for global disease detection and monitoring. As these systems matured, health officials increasingly applied them to detect other priority diseases, e.g. measles. The acute flaccid paralysis system is fully equipped with trained personnel and reporting mechanisms at national and subnational levels, either with designated surveillance medical officers and/or surveillance focal points to detect, report and respond to suspected cases. The surveillance system is supported by adequate laboratory facilities in national, regional or international laboratory networks. In many countries governments pay for the system from the national budget while in others the system is supported by resources from international organizations, partners and donors.

The system provides an infrastructure to monitor the incidence of Guillain-Barré syndrome in children younger than 15 years and to facilitate surveillance for Zika virus infection at all ages. Symptomatic cases of Zika virus infection present with symptoms like fever and rashes, which are common for measles, dengue and chikungunya; many countries have surveillance systems for such cases which can be adapted for Zika virus surveillance. A suggested process for using the acute flaccid paralysis surveillance system for Zika virus surveillance is presented in Annex 6.

Another example of a surveillance system that could be used in this way is the measles surveillance system. The Pan American Health Organization (PAHO) recommends the integration of measles and rubella surveillance because of the clinical similarities between these two infections. There are also other systems/tools which can be developed or adapted according to a country's needs and resources.

## 9. Event-based surveillance for arboviral diseases

### KEY ELEMENT 9.

Event-based surveillance is usually established to fill common and expected gaps in conventional surveillance. Timely collection and analysis of unstructured information from different sources (formal and informal), including from the health system itself, is the key to detecting and responding rapidly to signals/alerts coming from both within and outside the health sector.<sup>1,2</sup> The main objective of implementing event-based surveillance for arboviral infections transmitted by *Aedes* mosquitoes is early detection of clusters and outbreaks related to Zika, dengue, yellow fever or chikungunya in order to trigger actions and appropriate response measures.

### 9.1 Definition of event-based surveillance

Event-based surveillance is defined by WHO as the organized collection, monitoring, assessment and interpretation of mainly unstructured ad hoc information of health events or risks which may represent a potential acute risk to human health. Event-based surveillance is a functional component of early warning and response systems.<sup>3</sup>

<sup>1</sup> A guide to establishing event-based surveillance. Manila: WHO Regional Office for the Western Pacific; 2008 ([www.wpro.who.int/emerging\\_diseases/documents/docs/eventbasedsurv.pdf](http://www.wpro.who.int/emerging_diseases/documents/docs/eventbasedsurv.pdf), accessed 14 July 2018).

<sup>2</sup> Early warning and response to outbreaks and other public health events: a guide. New Delhi: WHO Regional Office for South-East Asia; 2008:SEA-CD-178.

<sup>3</sup> Early detection, assessment and response to acute public health events: implementation of early warning and response with a focus on event-based surveillance. Geneva: World Health Organization; 2014 ([https://www.who.int/ihr/publications/WHO\\_HSE\\_GCR\\_LYO\\_2014.4/en/](https://www.who.int/ihr/publications/WHO_HSE_GCR_LYO_2014.4/en/)).

## 9.2 Minimum requirements of event-based surveillance

Before an event-based surveillance system is implemented, the following components should be present:

- assessment/gap analysis of the existing system;
- clear definition of the data sources expected to be used;
- a dedicated information management mechanism (team/unit) responsible for capture, triage, verification, assessment and integrated coordination of each reported event triggering an immediate response;
- a list of the events that should trigger the system towards early detection of arboviruses;
- an operational event team/unit responsible at the central level with clear established channels of communication between the central level and the local staff and with the capacity to conduct a preliminary outbreak investigation; and
- preparation of rapid response capacities in the event of an important acute event being detected.

Event-based surveillance requires a multisectoral approach and should rely on sources of information beyond the traditional health system sources.<sup>1</sup>

## 9.3 Sources of information

In event-based surveillance for arboviral diseases, sources of information can be directly linked to the human health sector, but data can also be provided by the non-human health sector, local communities, media and international sources. The main potential sources of information and the channels of collection are presented in Annex 7. In comparison with syndromic surveillance, event-based surveillance relies on information from more unstructured, informal and ad hoc sources, as shown in Table 3.

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<sup>1</sup> Early detection, assessment and response to acute public health events: implementation of early warning and response with a focus on event-based surveillance. Geneva: World Health Organization; 2014 ([https://www.who.int/ihr/publications/WHO\\_HSE\\_GCR\\_LYO\\_2014.4/en/](https://www.who.int/ihr/publications/WHO_HSE_GCR_LYO_2014.4/en/)).

**Table 3.** Examples of sources of information used by syndromic surveillance and event-based surveillance systems for arboviral diseases

Source	Type of surveillance
The formal report by a health care worker of an increase in the number of suspected cases of yellow fever (according to the national case definition)	Syndromic surveillance system
The ad hoc report by a community leader of several deaths due to fever and jaundice among adults in his village (revealing a potential outbreak of yellow fever)	Event-based surveillance
The central pharmacy reports to the health authority that sales of anti-malaria drugs in non-endemic areas have exceeded the defined threshold	Syndromic surveillance system
A local pharmacy mentions to the local health authority that it is facing a shortage of anti-malaria drugs (medicine seldom sold in the shop) due to increased demand	Event-based surveillance
The notification by a country of the occurrence of locally acquired cases of dengue fever (a disease not previously present in the country) to neighbouring countries and WHO	Syndromic surveillance system
The ad hoc detection by country X that locally acquired dengue fever has been diagnosed in country Z (neighbouring and sharing the same ecosystem) through consulting the country's health ministry website	Event-based surveillance
The formalized exchange of zoonosis information between human and animal health sectors (e.g. intergovernmental initiative)	Syndromic surveillance system
The ad hoc use by a ministry of health of available crude veterinary information (i.e. all animal disease, including non-zoonosis) outside of any formalized frameworks	Event-based surveillance

**KEY ELEMENT 10.**

According to specific country needs, a number of mechanisms may be defined to collect information from formal and informal sources.

Countries often have limited resources, a situation which does not allow their surveillance systems to incorporate all potential reporting sources. Thus, reporting sources for event-based surveillance at country level should start with the most engaged sources and then extend progressively to other relevant sources.

#### **9.4 Examples of events captured by event-based surveillance for arboviral infection and the verification process**

Verification is defined by WHO as a proactive cross-checking of the validity of the signals collected by the early warning and response system contacting the original source and/or additional sources, or through field investigation. In the context of IHR (2005) (Article 10: verification), a State Party shall verify and provide WHO with information on events which may constitute a public health emergency of international concern occurring in the State's territory.

**KEY ELEMENT 11.**

The verification step in event-based surveillance is the process of identifying a relevant event which may constitute a public health threat. While the indicator-based surveillance process deals with data that have been validated previously, event-based surveillance focuses on non-validated information (rumour, media, etc.) that requires verification for validation. Verification is the process of confirming an event once the unofficial information has been reported or collected.

Information coming from different sources (formal and informal) should be verified. The verification process should be carefully structured in order to obtain valid data in a timely manner.

In this phase of the process information should be gathered by categorizing events such as: a cluster of fever and conjunctivitis (or other clinical symptoms/syndromes); death from arboviral disease or syndrome; an unusual increase in deaths, particularly in an array of fever and conjunctivitis (or other clinical symptoms/syndromes); and unexpected signs of microcephaly in the fetus or newborn. These categories and clusters constitute a potential public health event due to arboviral disease.

Depending on the source of information, the verification processes should consider establishing formal channels of communication for validation at national or local level in the case of unofficial information (e.g. media, community). Specific contact points at local level should be defined for the rapid verification of the information. Specific contact points for other sectors (vector control department, etc.) should be considered in order to facilitate multidisciplinary validation approaches when needed.

For information coming from official sources, the process of verification should follow the same steps as an investigation of an unusual event in the conventional system.

### ***9.5 Methods of reporting from the sources of information***

Ideally, all methods of immediate communication should be made available to those expected to participate in event-based surveillance. The most available and feasible methods are phone hotlines (call, SMS), toll-free numbers (green number) (call, SMS), email and fax. Examples of event reporting and investigating forms are given in Annex 8.

Reporting should be possible 24 hours a day, seven days a week.

### ***9.6 Specific surveillance strategy for early recognition of complications of Zika virus infection***

Neurological manifestations may appear in adults or older children during or after the acute phase of Zika virus infection. Guillain-Barré syndrome is the most frequent neurological complication. In its typical form, Guillain-Barré syndrome occurs as an ascending, progressive, symmetrical, subacute muscular paralysis that reaches peak severity by the fourth week and is accompanied by areflexia (absence of reflex).<sup>1</sup> For patients with suspected Guillain-Barré syndrome a complete clinical history and detailed neurological examination should be conducted.

<sup>1</sup> Guidelines for surveillance of Zika virus disease and its complications. Washington, DC: Pan American Health Organization, World Health Organization; 2016 Zika virus infection during pregnancy can cause infants to be born with microcephaly and other congenital malformations.

Zika virus infection during pregnancy can cause infants to be born with microcephaly and other congenital malformations (facial, craniofacial disproportion and other anthropometric disproportions). Microcephaly is defined as a head circumference more than 2 standard deviations below the reference population average standardized for age and sex.

#### KEY ELEMENT 12.

Strategic surveillance for early recognition of complications associated with Zika virus infection should focus on Guillain-Barré syndrome and microcephaly.

- Guillain-Barré syndrome
  - Review the existing sources of information (clinical records in the health system) in order to establish a baseline incidence of Guillain-Barré syndrome.
  - Review the surveillance data on acute flaccid paralysis, which can be used as a proxy indicator of Guillain-Barré syndrome.
- Microcephaly
  - Establish a baseline and monitor the prevalence of birth defects and trends for microcephaly.
  - Investigate any sudden increase in the number of cases of microcephaly at birth.

## 10. How vector surveillance can help in early detection

Vector-borne diseases pose a particular challenge to national public health authorities because of their complex nature, requiring multidisciplinary competencies and strong rapid interaction among the sectors involved. *Aedes* mosquitoes have been found in at least eight countries of the Region, while their presence or absence is still to be assessed in the rest of the area. Consequently, a strong entomological surveillance system is needed in the Region.

Mosquito surveillance is a key component of any local integrated vector management programme (e.g. the malaria programme). Vector control is an essential component of malaria prevention and has been proven to successfully reduce or interrupt malaria transmission when coverage is sufficiently high.

Preventing or limiting the transmission of dengue, chikungunya, yellow fever and Zika viruses is completely dependent on the control of mosquito vectors and the reduction of person/mosquito contact. *Aedes aegypti* and *Ae. albopictus* are the mosquito species incriminated/suspected as vectors of arboviral diseases. Entomological sampling methods to assess the *Aedes* population density and evaluate control interventions have been implemented in many Asian countries. There is a need to introduce and adapt these methods in the Eastern Mediterranean Region.

There is also a strong need to build/strengthen an early warning system to pre-empt/predict and early detect vector-borne diseases in the Region through integrating vector surveillance with syndromic surveillance and event-based surveillance. Efficient use of the surveillance data is also needed to pre-empt/predict and early detect transmission risk. Operational research needs to be conducted to determine the thresholds for entomological indices that can be useful in pre-empting and predicting the occurrence of epidemics. In addition, entomological surveillance needs to be purposeful and aligned with risk assessment in the process of early detection of virus circulation or to detect the introduction of competent vectors.

Countries are advised to adopt an integrated vector management approach addressing all vector-borne diseases; this is in line with resolution EM/RC52/R.6 on integrated vector management adopted by the WHO Regional Committee for the Eastern Mediterranean in 2005. Integrated vector management focuses strongly on programme management using vector surveillance and clinical surveillance/notifiable disease, which will be used for guidance on the impact of interventions. Countries need further guidance on which vector control interventions to use in specific contexts (prevention, epidemic etc.).

#### KEY ELEMENT 13.

Integration of entomological surveillance into syndromic and event-based surveillance systems will help in early detection of arboviral diseases.

Entomological surveillance that would provide useful inputs into syndromic and event-based surveillance systems:

- numbers and geographical distribution of mosquitoes over time;
- data on high-density infestations of mosquitoes that have occurred;
- data on the periods when mosquito populations have increased;
- data on the mosquito population's susceptibility to insecticides.

In addition, entomological surveillance is a critical component of prevention and control programmes as it provides the information necessary for risk assessment, epidemic response and programme evaluation.<sup>1</sup>

Operational activities for entomological surveillance of Zika virus are presented in Annex 9.

## 11. Laboratory role and services

#### KEY ELEMENT 14.

Laboratory confirmation is a key component of surveillance, but appropriate resources need to be allocated and training provided.

#### KEY ELEMENT 15.

Only a proportion of cases of targeted syndromes should be sampled at the community level.

- All severe cases that require hospitalization should be tested.
- Laboratory tests are important to establish epidemiological links, and can also be an important source of information for early detection of arboviral diseases.

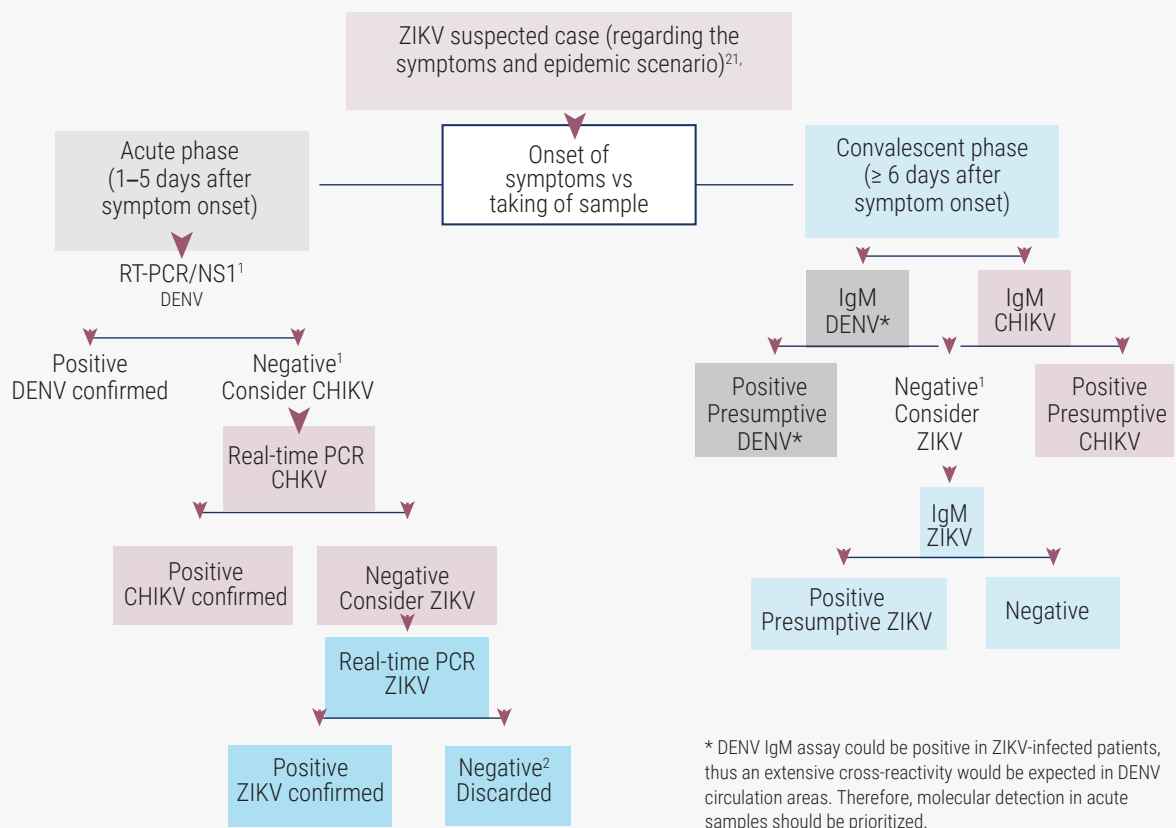
Once syndromic surveillance is in place for arboviral diseases it is important to establish laboratory services. Routine laboratory-based surveillance complements the syndromic surveillance system, and is needed to confirm the disease and start control strategies.

<sup>1</sup> Entomological surveillance for *Aedes* spp. in the context of Zika virus: interim guidance for entomologists. Geneva: World Health Organization; 2016 (<https://www.who.int/csr/resources/publications/zika/aedes-entomological-surveillance>).

Laboratory confirmation tests should be considered in patients with acute onset of fever, maculopapular rash, arthralgia or conjunctivitis who live in or have travelled to an area with ongoing transmission in the two weeks preceding the onset of illness.

Diagnostic tests for confirming the presence of one of the targeted arboviral diseases should be available in the central reference laboratory of the country.

The algorithm presented in Fig. 2 is addressed to reference laboratories with established capacity (molecular/antigenic and serological) to detect dengue, chikungunya<sup>1</sup>, and Zika<sup>2</sup> viruses. A biosafety level 2 containment laboratory is required to handle suspect samples.



CHIKV = chikungunya virus; DENV = dengue virus; ZIKV = Zika virus

<sup>1</sup> This algorithm is not exhaustive, and dengue infection should be discarded according to the clinical management guidelines and the laboratory-specific algorithm.

<sup>2</sup> These recommendations are subject to modifications that take into account advances in knowledge of the disease and the etiologic agent.

Source: Zika virus (ZIKV) surveillance in the Americas: interim guidance for laboratory detection and diagnosis. Washington (DC): Pan American Health Organization; 2015 ([http://iris.paho.org/xmlui/bitstream/handle/123456789/18602/zikavirusinterim\\_jan2015.pdf?sequence=1&isAllowed=y](http://iris.paho.org/xmlui/bitstream/handle/123456789/18602/zikavirusinterim_jan2015.pdf?sequence=1&isAllowed=y)).

**Fig. 2.** Algorithm for detecting Zika, dengue and chikungunya viruses

## 12. Integration of syndromic surveillance and event-based surveillance

The structure of the syndromic surveillance and event-based systems should be designed to be complementary to the conventional system, and implemented within the communicable disease surveillance system in an integrated way.

The main components of the overall surveillance (syndromic and routine) system have to be simple and practical to be functional, and should be maintained over time. Approaches towards integration depend on the situation in each country. An approach towards integrating the syndromic surveillance and event-based surveillance within the conventional surveillance system could include the following:

- Integrate surveillance of Zika and other arboviral diseases into the notifiable diseases list as diseases under surveillance.
- Identify the probable and confirmed case definitions for Zika and other arboviral diseases in addition to targeted syndromes as suspect cases of *Aedes*-borne diseases.
- Train public health professionals on the syndromic surveillance process and insist that, even in the absence of suspected or confirmed Zika or other arboviral infectious diseases, health centres responsible for surveillance report on a weekly basis<sup>1</sup> (e.g. 0 case of syndromes sensitive to Zika) during the season of high risk transmission, just as they would do for mandatory diseases (e.g. acute flaccid paralysis) in the conventional surveillance system.

## 13. Main challenges for implementation

To apply the syndromic surveillance and event-based surveillance systems appropriately at country level, there are several important challenges that need to be considered.

- Technical challenges:
  - limited political, technical, bureaucratic and leadership commitment;
  - high sensitivity and low specificity of the surveillance system;
  - absence of integration of the surveillance system;
  - poor data source accessibility;
  - low accuracy and incompleteness of the surveillance system;
  - poor integration of research into the system, mainly at inception and during operations;
  - lack of mechanisms for intersectoral collaboration with other concerned partners (entomological department, etc.); and
  - limited laboratory capabilities.

<sup>1</sup> The weekly reporting rate, calculated as the proportion of reporting health centres that sent in their surveillance report on time even in the absence of cases, was successfully used to eradicate poliomyelitis and is an effective tool for assessing surveillance compliance at the local level.



- Human resource challenges:
  - absence of a dedicated data management team for the system (e.g. health workers involved in the surveillance may feel exhausted by additional work);
  - little relevant training, monitoring and supervision linked to the early detection process;
  - lack of trained workforce at each level (staff turn-over, etc.); and
  - low level of community participation.
- Financial challenges:
  - insufficient financial support, especially at intermediate and lower levels for response activities.

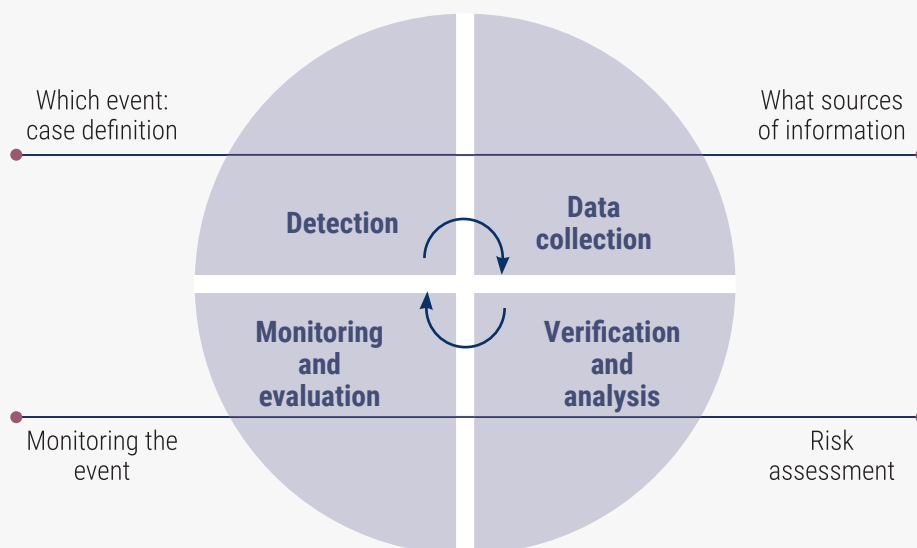
## 14. Strategic requirements to implement/strengthen the system

To implement or strengthen the syndromic surveillance system and event-based surveillance at country level, there are several strategic requirements.

- Technical requirements:
  - Optimal data sources for the syndromic surveillance system and event-based surveillance need to be identified and systematically assessed.
  - Syndrome definitions that indicate high performance outbreak detection need to be developed and validated.
  - Detection methods should formally integrate multiple disparate data sources over space and time.
  - Rigorous data management methods should be applied and formalized.
  - After the surveillance system has been designed and put into operation it should not be used only for early detection of Zika and other arboviral disease outbreaks but for the detection of other emerging and re-emerging infectious diseases.
  - Constant evaluation is required of the performance of detection and monitoring systems and training and validation data containing signal and noise.
  - Technical partnerships and intersectoral collaboration.
- Human resource requirements:
  - staff management and redeployment; and
  - training on data for the entire early detection process.
- Financial requirements:
  - advocacy for financial support.

## 15. Practical requirements for running the system

Fig. 3 shows the main components of event-based surveillance, starting with the detection of the event, through data collection and analysis, and finishing with monitoring and evaluation. This is repeated to maintain a continuous process for early detection of events.



**Fig. 3.** Main components of event-based surveillance

#### KEY ELEMENT 16.

To establish event-based surveillance within the existing surveillance system, certain practical steps need to be followed taking into account the components of event-based surveillance.

Seven steps can be trialled to establish event-based surveillance for arboviral diseases:

1. Identify the main events to detect.
2. Determine the sources of information.
3. Set up a dedicated data management structure for event-based surveillance.
4. Establish simple procedures for verification, analysis and interpretation.
5. Link to response mechanism.
6. Develop the monitoring and evaluation process.
7. Provide feedback.

After the alert signal is received, the process of syndromic surveillance and event-based surveillance systems will follow the main operational and technical steps:

- Verification of the alert signal is usually completed in the investigation process in surveillance for response. However, for event-based surveillance, the investigation may follow other informal and unstructured methods to verify data coming from different sources. In addition, the verification process may sometimes properly integrate disparate data of the event.
- Systematic risk assessment and risk analysis should then be completed for all available reliable data on the outbreak.

- Regular risk communication about any update of the surveillance and response for the outbreak should be implemented between the concerned health officials, decision-makers, stakeholders and partners.
- Practical steps taken should highlight the importance and need for training.

## 16. Monitoring and evaluation of the system

Monitoring and evaluation of both syndromic surveillance and event-based surveillance systems for arboviral diseases help in ensuring the continuous performance of the system and should be established when the system is being designed. Monitoring and evaluation processes are essential to ensure that the system is well established and functioning correctly.

Major adaptations may be carried out according to changes in the system (expected or unexpected). Regular monitoring and evaluation of the performance of the event-based surveillance system should be undertaken. At least two events per year are evaluated from notification to confirmation/assessment and response.<sup>1</sup>

### KEY ELEMENT 17.

To ensure the sustainability of the performance of the surveillance system the quality of the data reported should be monitored rigorously. This includes the proportion of investigations that included a visit to the patient's home within 48 hours of notification of a suspected case, the proportion of suspected cases where a blood sample was obtained within 30 days of the onset of the rash, the proportion of samples received by the reference laboratory within five days of being obtained, the percentage of laboratory results reported within four days of receipt of the sample, and the proportion of cases discarded on the basis of a laboratory test. It is recommended that compliance with all indicators is at least 80%.

In the monitoring and evaluation step it is important to identify certain indicators:

- review after major events
- percentage of reports received and assessed within 24 hours
- timeliness, completeness
- assessment of the system every two years
- an in-built feedback system.

<sup>1</sup> A guide to establishing event-based surveillance. Manila: WHO Regional Office for the Western Pacific; 2008 ([www.wpro.who.int/emerging\\_diseases/documents/docs/eventbasedsur.pdf](http://www.wpro.who.int/emerging_diseases/documents/docs/eventbasedsur.pdf), accessed 14 July 2018).

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## Annexes

### Annex 1. Main epidemiological and clinical characteristics of Zika virus, dengue and chikungunya

Organism/ disease	Zika virus	Dengue	Chikungunya
<b>Agent</b>	Single-stranded RNA virus of the Flaviviridae family, genus <i>Flavivirus</i>	Single-stranded RNA viruses of the Flaviviridae family, genus <i>Flavivirus</i> , with four serotypes (DENV-1, DENV-2, DENV-3 and DENV-4)	Single-stranded RNA virus of the Togaviridae family, genus <i>Alphavirus</i>
<b>Transmission</b>	<p>Through the bite of infected <i>Aedes</i> mosquitoes</p> <p>Intrauterine, perinatal, sexual, laboratory</p> <p>Possible transfusion-associated transmission</p> <p>Zika viral particles have been found in breast milk but transmission through breastfeeding has not been documented</p>	<p>Through the bite of infected <i>Aedes</i> mosquitoes, primarily <i>Ae. aegypti</i> and <i>Ae. albopictus</i></p> <p>Because of the approximately 7-day viraemia in humans, bloodborne transmission is possible through exposure to infected blood, organs or other tissues</p> <p>Perinatal transmission occurs; highest risk appears to be among infants whose mothers are viraemic at the time of delivery</p> <p>Possible transmission through breast milk</p>	<p>Through the bite of infected <i>Aedes</i> mosquitoes, primarily <i>Ae. aegypti</i> and <i>Ae. albopictus</i></p> <p>Transmission occurs during outbreaks of the disease</p> <p>Bloodborne transmission is possible</p> <p>Possible maternal–fetal transmission when mothers are viraemic at the time of delivery</p> <p>CHIKV has not been found in breast milk</p>

Organism/ disease	Zika virus	Dengue	Chikungunya
<b>Epidemiology</b>	<p>First identified in Uganda in 1947</p> <p>Prior to 2007, only sporadic human disease cases from countries in Africa and Asia</p> <p>In 2007, there was a ZIKV disease outbreak in the Federated States of Micronesia; in subsequent years outbreaks of ZIKV occurred in countries in South-East Asia and the Western Pacific</p> <p>In 2015, ZIKV appeared in the Western hemisphere with large outbreaks reported in Brazil</p> <p>Since then, the virus has spread throughout much of the Americas</p>	<p>Dengue endemic illness occurs in &gt; 100 countries worldwide.</p> <p>Although the geographic distribution of dengue is similar to that of malaria, dengue is more of a risk in urban and residential areas than malaria. DengueMap (<a href="http://www.healthmap.org/dengue/index.php">www.healthmap.org/dengue/index.php</a>) shows up-to-date information on areas of ongoing transmission</p>	<p>Often causes large outbreaks with high attack rates, affecting one third to three quarters of the population in areas where the virus is circulating. Outbreaks have occurred in Africa, Asia, Europe and islands in the Indian and Pacific oceans.</p> <p>In late 2013, the first locally acquired cases were recorded in the Americas on islands in the Caribbean. Given the high level of viraemia in humans and the worldwide distribution of <i>Ae. aegypti</i> and <i>Ae. albopictus</i>, there is a risk of importation into new areas by infected travellers</p>
<b>Reservoir of the virus</b>	<p>Mosquito-borne <i>Flavivirus</i> is closely related to the dengue virus. While mosquitoes are the vector the reservoir species remains unknown, although serological evidence has been found in West African monkeys and rodents</p>	<p>Humans are the only vertebrate hosts of the virus. There is a jungle cycle between monkeys and mosquitoes, but this plays no role in human disease</p>	<p>Humans and monkeys are the main hosts but the range of vertebrate hosts is not well understood. The possibility of Australian animal species acting as hosts has not been determined; recently, bats have been indicated as a possible host</p>
<b>Cycle of transmission</b>	<p>Transmitted from human to human by the bites of infected mosquitoes. It is thought that the mosquito contracts the virus when it bites an infected person. The mosquito is then infective for the rest of its life and can spread the virus every time it bites someone</p>	<p>Transmitted from human to human by the bites of infected mosquitoes. It is thought that the mosquito contracts the virus when it bites an infected person. The mosquito is then infective for the rest of its life and can spread the virus every time it bites someone</p>	<p>Transmitted from human to human by the bites of infected mosquitoes. These mosquitoes are active throughout daylight hours, and there may be peaks of activity in the early morning and late afternoon. Both species are found biting outdoors, but <i>Ae. aegypti</i> will also readily feed indoors</p>

Organism/ disease	Zika virus	Dengue	Chikungunya
<b>Clinical signs</b>	<p>Most infections are asymptomatic</p> <p>Symptomatic infections are generally minor</p> <p>Commonly reported signs and symptoms include fever, maculopapular rash, arthralgia and conjunctivitis</p> <p>Other symptoms include myalgia, headache and vomiting</p> <p>Zika virus RNA was identified in tissues from several infants with microcephaly and from fetal losses in women who were infected during pregnancy</p> <p>Guillain-Barré syndrome also has been reported in some patients after Zika virus infection</p>	<p>About 75% of all infections are asymptomatic</p> <p>Symptomatic infection most commonly presents as a mild to moderate, nonspecific, acute, febrile illness</p> <p>Up to 5% of all dengue patients develop severe, life-threatening disease</p> <p>Early clinical findings are nonspecific but require a high index of suspicion because recognizing early signs of shock and promptly initiating intensive supportive therapy can reduce the risk of death among patients with severe dengue from 10% to &lt; 1%</p> <p>Dengue begins abruptly after an incubation period of 5–7 days (range 3–10 days), and the course follows 3 phases: febrile, critical and convalescent. Fever typically lasts 2–7 days and can be biphasic</p> <p>Other signs and symptoms may include severe headache; retro-orbital pain; muscle, joint, and bone pain; macular or maculopapular rash; minor haemorrhagic manifestations, including petechiae, ecchymosis, purpura, epistaxis, bleeding gums, haematuria, and a positive tourniquet test result</p> <p>Some patients have injected oropharynx and facial erythema in the first 24–48 hours after onset</p> <p>Warning signs of progression to severe dengue occur in the late febrile phase, around the time of defervescence, and include persistent vomiting, severe abdominal pain, mucosal bleeding, difficulty breathing, signs of hypovolemic shock and rapid decline in platelet count with an increase in haematocrit (haemoconcentration)</p>	<p>3–28% of people infected remain asymptomatic</p> <p>For people who develop symptomatic illness, the incubation period is typically 3–7 days (range 1–12 days). Disease is most often characterized by sudden onset of high fever (temperature typically &gt; 39 °C) and joint pains</p> <p>Other symptoms may include headache, myalgia, arthritis, conjunctivitis, nausea, vomiting or a maculopapular rash</p> <p>Fevers typically last from several days up to 1 week; the fever can be biphasic</p> <p>Joint symptoms are often severe and can be debilitating. They occur most commonly in hands and feet but can affect more proximal joints</p> <p>Rash usually occurs after onset of fever</p>



Organism/ disease	Zika virus	Dengue	Chikungunya
<b>Diagnostic</b>	<p>Considered in patients with acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis who live in or have travelled to an area with ongoing transmission in the 2 weeks preceding onset of illness</p> <p>In suspected Zika virus disease, rRT-PCR should be performed on urine specimens collected &lt; 14 days after onset of symptoms and serum specimens collected &lt; 7 days after onset of symptoms. A positive rRT-PCR result confirms Zika virus infection, and no antibody testing is indicated</p> <p>Serum IgM antibody testing should be performed if rRT-PCR is negative or for samples collected <math>\geq</math> 7 days after illness onset. However, these serologic assays can be positive because of cross-reacting antibodies against related Flaviviruses (such as dengue or yellow fever viruses)</p> <p>Virus-specific neutralization testing can be used to discriminate between cross-reacting antibodies in primary Flavivirus infections, although neutralizing antibodies might still yield cross-reactive results in people who were previously infected or vaccinated against a related Flavivirus (secondary Flavivirus infection)</p>	<p>Considered in a patient who was in an endemic area within the 2 weeks prior to onset of symptoms</p> <p>Laboratory confirmation can be made from a single acute-phase serum specimen obtained early (<math>\leq</math> 5 days after fever onset) in the illness by detecting DENV genomic sequences with RT-PCR or DENV NS1 antigen by immunoassay</p> <p><math>\geq</math> 4 days after fever onset, IgM anti-DENV can be detected with ELISA</p> <p>For patients presenting during the first week after fever onset diagnostic testing should include a test for DENV (PCR or NS1) and IgM anti-DENV</p> <p>&gt; 1 week after onset of fever, IgM anti-DENV is most useful, although NS1 has been reported positive up to 12 days after fever onset</p> <p>Presence of DENV by PCR or NS1 antigen in a single diagnostic specimen is considered laboratory confirmation of dengue in patients with a compatible clinical and travel history</p> <p>IgM anti-DENV in a single serum sample suggests a probable, recent DENV infection and should be considered diagnostic for dengue if the infection most likely occurred in a place where other potentially cross-reactive flaviviruses (such as West Nile, yellow fever, and Japanese encephalitis viruses) are not a risk</p> <p>IgM anti-DENV seroconversion in acute- and convalescent-phase serum specimens is considered laboratory confirmation of dengue</p>	<p>Preliminary diagnosis is based on the patient's clinical features, places and dates of travel, and activities</p> <p>Laboratory diagnosis is generally accomplished by testing serum to detect virus, viral nucleic acid, or virus-specific IgM and neutralizing antibodies</p> <p>During the first week after onset of symptoms, CHIKV infection can be diagnosed by performing viral culture or nucleic acid amplification on serum</p> <p>CHIKV-specific IgM and neutralizing antibodies normally develop toward the end of the first week of illness</p> <p>Convalescent-phase samples should be obtained from patients whose acute-phase samples test negative</p>



Organism/ disease	Zika virus	Dengue	Chikungunya
		IgG anti-DENV by ELISA in a single serum sample is not useful for diagnostic testing because it remains detectable for life after a DENV infection. In addition, people infected with or vaccinated against other flaviviruses may produce cross-reactive Flavivirus antibodies, yielding false-positive serologic dengue diagnostic test results	
<b>Differential diagnosis</b>	Dengue, chikungunya, malaria, rubella, measles, parvovirus, adenovirus, enterovirus, leptospirosis, rickettsiosis, and group A streptococcal infections	Zika, chikungunya, malaria, West Nile fever, yellow fever and Japanese encephalitis	Dengue, Zika, malaria, leptospirosis, parvovirus, enterovirus, group A streptococcus, rubella, measles, adenovirus, postinfection arthritis, rheumatologic conditions, and alphavirus infections
<b>Reporting cases</b>	Health care providers should report suspected and confirmed cases to their state or local health departments. Zika virus disease is a nationally reportable disease	All suspected cases should be reported to the local health department because dengue is a nationally reportable disease	Health care providers should report suspected and confirmed cases to their state or local health departments to facilitate diagnosis and mitigate the risk of local transmission Reporting should be done within 5 days of diagnosis

Organism/ disease	Zika virus	Dengue	Chikungunya
<b>Complications</b>	<p>Complications are rare, but can be severe and debilitating</p> <p>Zika virus infection can trigger Guillain-Barré syndrome</p> <p>Possible complications of Zika virus infection in pregnancy are of particular concern (microcephaly and other congenital fetal neurological disorders) and fetal death is also possible</p>	<p>The critical phase of dengue begins at defervescence and typically lasts 24–48 hours.</p> <p>Most patients clinically improve during this phase, but those with substantial plasma leakage develop severe dengue</p> <p>Patients with severe plasma leakage have pleural effusions or ascites, hypoproteinemia and haemoconcentration</p> <p>Patients may appear to be well despite early signs of shock</p> <p>Severe haemorrhagic manifestations, including haematemesis, bloody stool, melaena, or menorrhagia, especially if they have prolonged shock</p> <p>Atypical manifestations include hepatitis, myocarditis, pancreatitis, and encephalitis</p>	<p>Rare but serious complications can occur, including myocarditis, ocular disease (uveitis, retinitis), hepatitis, acute renal disease, severe bulbous lesions, and neurologic disease such as meningoencephalitis, Guillain-Barré syndrome, myelitis or cranial nerve palsies</p> <p>Some patients will have a relapse of rheumatologic symptoms such as polyarthralgia, polyarthritis, tenosynovitis or Raynaud syndrome months after acute illness</p> <p>Intrapartum transmission: complications for the baby can occur, including neurologic disease, haemorrhagic symptoms and myocardial disease</p>

PCR: polymerase chain reaction  
 ELISA: enzyme-linked immunosorbent assay  
 NS1: nonstructural protein 1

**Risk for travellers:** Travellers at increased risk of more severe disease, including those with underlying medical conditions and women in late pregnancy, should consider avoiding travel to areas with ongoing outbreaks. The risk increases the longer the duration of travel and the greater the disease incidence in the travel destination. If travel is unavoidable protective measures against mosquito bites should be taken.

- Select accommodation with well-screened windows and doors or air conditioning when possible.
- *Aedes* mosquitoes typically live indoors and are often found in dark, cool places such as closets, under beds, behind curtains, in bathrooms and on porches.
  - Use insecticides to get rid of mosquitoes in these areas.
- Wear clothing that adequately covers the arms and legs, especially during the early morning and late afternoon when the risk of being bitten is highest.
- Use insect repellent.

**Annex 2.** *Classification of case definitions of Zika, dengue and chikungunya*

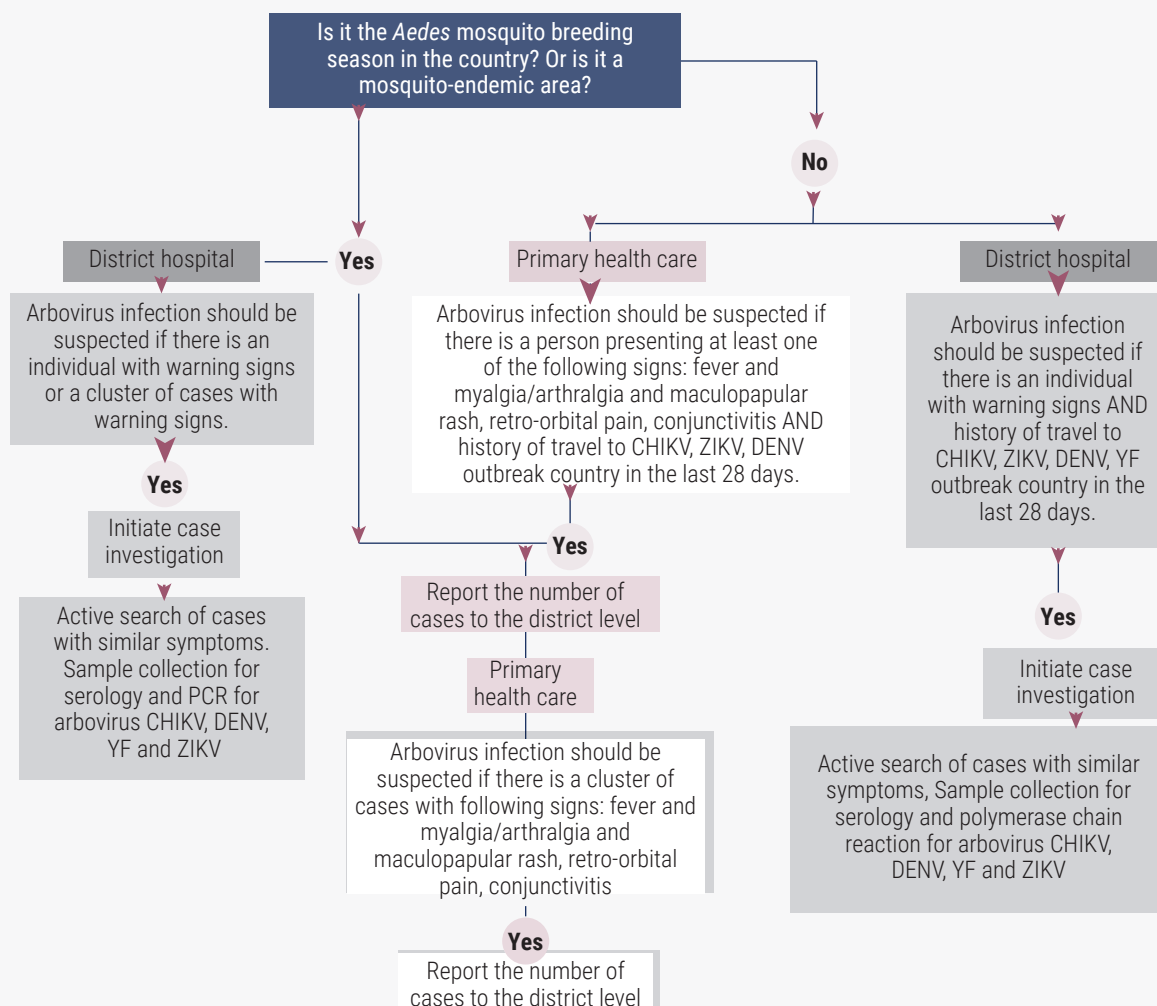
Disease	Classification	Required sign	Conditional sign
<b>Zika</b>	Suspected case	Maculopapular rash	At least one of the following signs: moderate fever, arthralgia/ arthritis, conjunctivitis (non-purulent/hyperaemia), periarticular swelling
	Confirmed case	Molecular test: presence of ZIKV RNA in blood or other samples (e.g. urine, saliva) Immunological test	
<b>Dengue</b>	Dengue without warning signs	Fever	Two of the following: nausea/ vomiting, rash, aches and pain, leukopenia, positive tourniquet test
	Dengue with warning signs	One of the following: abdominal pain/tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy/ restlessness, liver enlargement > 2 cm, increase in haematocrit concurrent with rapid increase in platelet count	
	Severe dengue	One of the following: severe plasma leakage leading to shock and fluid accumulation with respiratory distress, severe bleeding, severe organ involvement	
<b>Chikungunya</b>	Acute clinical case	Fever (> 38.5 °C)	Epidemiological criterion or laboratory criterion (polymerase chain reaction, serology, viral culture)
	Atypical case	Clinical case of laboratory-confirmed CHIKV accompanied by other manifestations (e.g. neurological)	
	Severe acute case	Clinical case of laboratory confirmed CHIKV presenting dysfunction of ≥ 1 organ or system that threatens life and requires hospitalization	

### Annex 3. Examples of surveillance and control measures for *Aedes* mosquitoes

Before mosquito season	Beginning of mosquito season
<ul style="list-style-type: none"> <li>■ Conduct public mosquito education campaigns focusing on reducing or eliminating larval habitats for the <i>Ae. aegypti</i> and <i>Ae. albopictus</i> vectors.</li> <li>■ Conduct surveys to determine abundance, distribution and type of containers; large numbers of containers may translate into high mosquito abundance and high risk.</li> <li>■ Initiate a community-wide source reduction campaign – the goal of the campaign is to motivate the community to remove and dispose of any water-holding containers.</li> <li>■ Cover, dump, modify or treat large water-holding containers with long-lasting larvicide.</li> <li>■ Reduce adult mosquito resting sites by keeping vegetation trimmed and tall grass cut.</li> <li>■ Develop mosquito education materials about <i>Ae. aegypti</i> and <i>Ae. albopictus</i> and personal protection measures.</li> </ul>	<ul style="list-style-type: none"> <li>■ Continue public education campaigns focusing on reducing or eliminating larval habitats for <i>Ae. aegypti</i> and <i>Ae. albopictus</i> vectors.</li> <li>■ Continue to distribute mosquito education materials about <i>Ae. aegypti</i> and <i>Ae. albopictus</i> and personal protection measures.</li> <li>■ Initiate <i>Ae. aegypti</i> and <i>Ae. albopictus</i> community-wide surveys to:               <ul style="list-style-type: none"> <li>▪ determine presence or absence</li> <li>▪ estimate relative abundance</li> <li>▪ determine distribution</li> <li>▪ develop detailed vector distribution maps.</li> </ul> </li> <li>■ Evaluate the efficacy of source reduction and larvicide treatment.</li> <li>■ Continue/maintain community source reduction efforts.</li> <li>■ Initiate adult sampling to identify or confirm areas of high adult mosquito abundance.</li> <li>■ Initiate preventive adult control to reduce adult populations, targeting areas of high mosquito abundance.</li> <li>■ Concentrate control efforts around places with high mosquito density.</li> </ul>

Source: Surveillance and control of *Aedes aegypti* and *Aedes albopictus* in the United States. Atlanta: Centers for Disease Control and Prevention; 2015 (<https://www.cdc.gov/chikungunya/pdfs/Surveillance-and-Control-of-Aedes-aegypti-and-Aedes-albopictus-US.pdf>, accessed 5 March 2019).

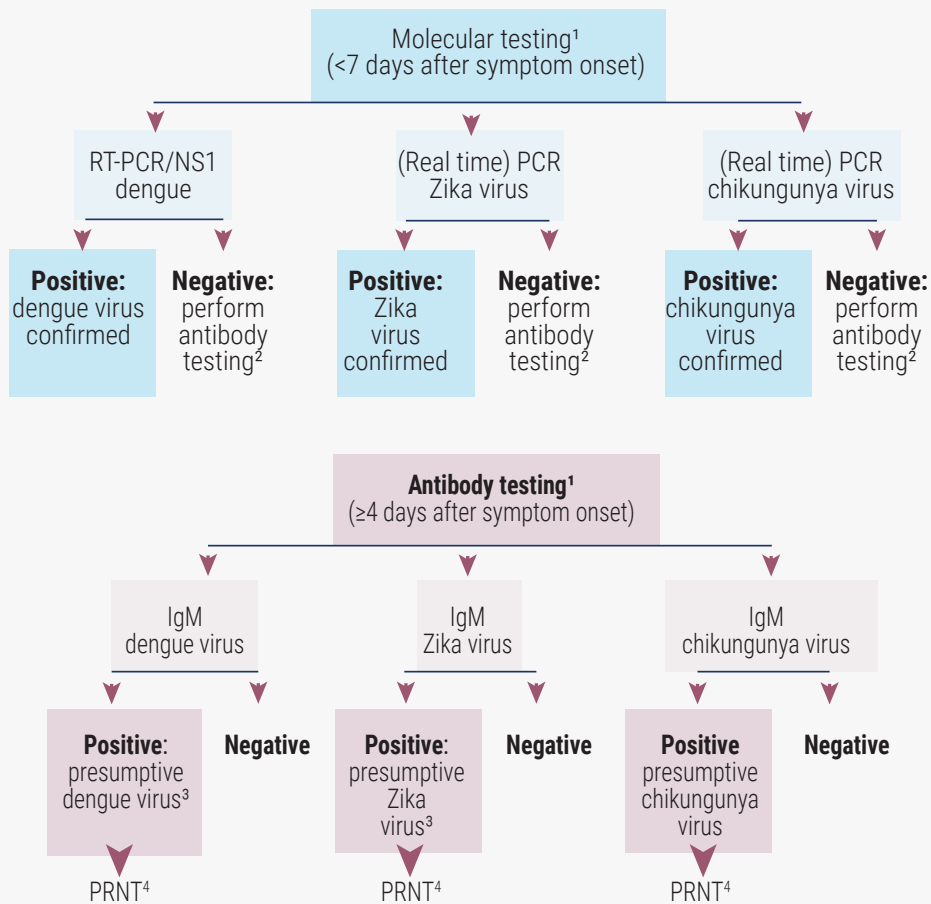
**Annex 4.** Algorithm for data flow for a syndromic surveillance system in the event of any arboviral disease being detected



PCR = polymerase chain reaction; CHIKV = chikungunya virus; DENV = dengue virus; YF = yellow fever; ZIKV = Zika virus

## Annex 5. Algorithm for arbovirus detection for suspected cases of dengue, Zika or chikungunya

Tiered algorithm for arbovirus detection for suspected cases of chikungunya, dengue, or Zika (Testing only performed if travel history indicates travel to affected area.)



<sup>1</sup> Due to extensive cross-reactivity in Flavivirus serological assays, for samples collected <7 days post illness onset, molecular detection should be performed first.

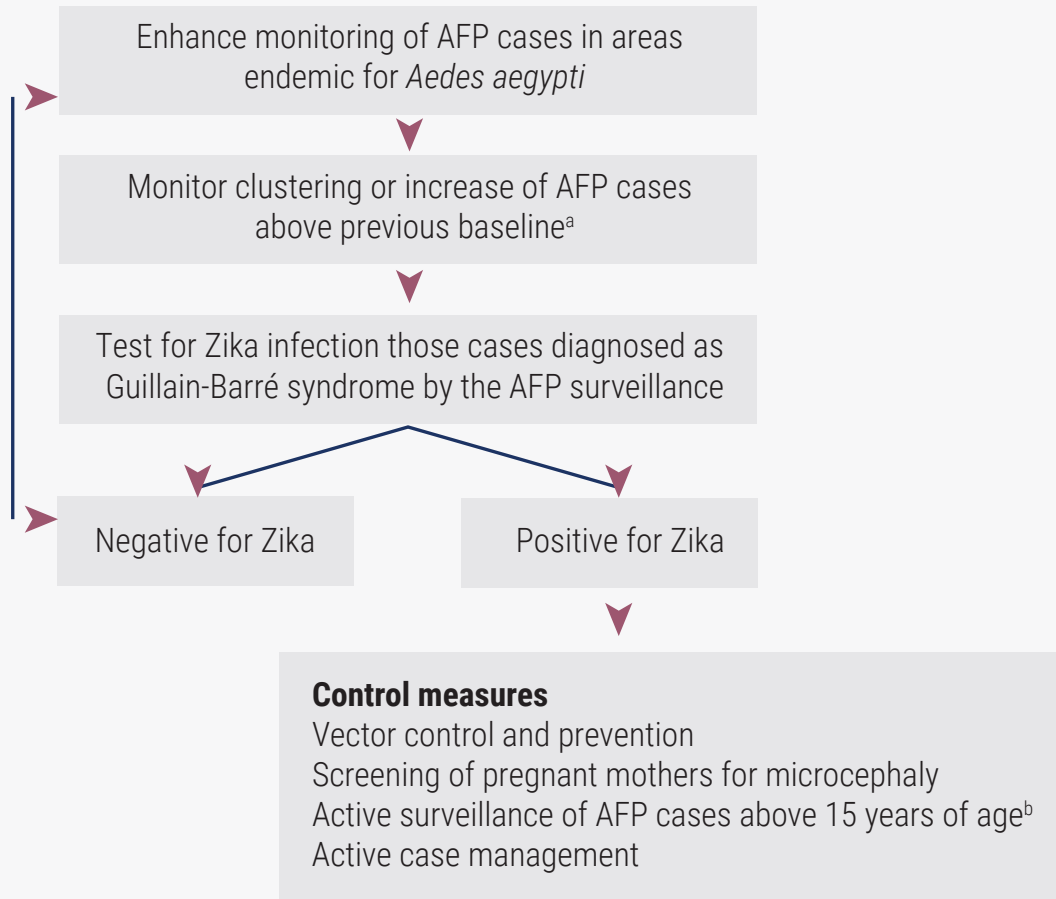
<sup>2</sup> Perform if sample ≥4 days after symptom onset.

<sup>3</sup> Extensive cross-reactivity would be expected in samples from DENV/ZIKV circulation areas. A positive IgM assay with either antigen should be confirmed by using PRNT against both ZIKV and DENV as well as any other flavivirus (eg. ZIKV, WNV, etc.) that might be found in that geographic area (including travel areas).

<sup>4</sup> PRNT (plaque reduction neutralization test) should include any Flavivirus (eg. ZIKV, WNV, etc.) that might be found in that geographic area (including travel areas).

Source: Memorandum – Subject: Revised diagnostic testing for Zika, chikungunya, and dengue viruses in US Public Health Laboratories – February 7, 2016. Atlanta: Centers for Disease Control and Prevention; 2016 (<https://stacks.cdc.gov/view/cdc/38149>, accessed 13 February 2019).

## Annex 6. Suggested process for using the acute flaccid paralysis (AFP) surveillance system for Zika virus surveillance



<sup>a</sup>Countries have a set yearly AFP target rate to find AFP cases for polio surveillance. This provides the baseline for AFP cases in the population younger than 15 years.

<sup>b</sup>Although AFP surveillance is for children under 15 years of age, it can be used as a proxy early warning monitoring system for AFP cases in all ages.

Source: Kandel N, Lamichhane J, Tangermann RH, Rodier GR. Detecting Guillain-Barré syndrome caused by Zika virus using systems developed for polio surveillance. Bull World Health Organ. 2016 Sep 1;94(9):705–8. PMID:27708476.

**Annex 7. Potential sources of information and means of collection**

Potential source	Rationale	Potential channel for information
<b>Health sources</b>		
National institutes of public health and reference laboratories; local and regional health authorities Public health institutions responsible for drugs, poison control centres, primary care facilities, hospitals, public and private sector, laboratories, health services in prisons, main health insurance companies	First line of information in event-based surveillance and can also provide structured information from indicator-based surveillance as part of routine surveillance	Direct contact (visit sources); Consultation reports Phones and applications: SMS, smartphone apps Internet: email, social networks (WhatsApp, twitter, Facebook, etc.) Systematic consultation of the written and digital press Internet: monitoring information
Community medicine and community health workers	These are preferred sources of information because of their links with local communities and their presence in the field, particularly in isolated areas where access to primary health care is limited	
Entomological departments	A health event linked to circulating vectors may pose a potential threat to human health	
Traditional medicine	In some areas, the population using traditional medicine can be a valuable source of information	
Organizations of medication procurement and pharmacy sales	Drug sales can be an indicator of the appearance of diseases, e.g. drugs for acute febrile illness. Monitoring can help identify new pathogens or spread of a pathogen in a new area	



Potential source	Rationale	Potential channel for information
<b>Non-health sources</b>		
National sources: ministries of agriculture, education, environment, foreign affairs, customs and employment; civil society, nongovernmental organizations, etc.	The validity of the information is based on the fact that these are official sources, e.g. notification by the school system of an unexpected level of absenteeism among students or children can be used as an indicator of the onset of a disease	Direct contact (visit sources) Consultation reports Phones and applications: SMS, smartphone apps Internet: email, social networks (WhatsApp, twitter, Facebook, etc.)
Meteorological and air quality	Observations or forecasts of extreme temperatures (i.e. cold or hot spells) must be reported	Systematic consultation of the written and digital press Internet: monitoring information
Work place, industry and educational institutions	Reports from the work place, including private industry, indicating a high level of absenteeism among employees can also be used as indicators of new pathogens or spread of a pathogen in the area.	
Community leaders and civil society (religious leaders, etc.)	These individuals or groups can report unusual health events observed in their communities informally	
<b>Media</b>		
National and international media (audiovisual, internet)	Local, national and international media are important sources of information Clusters of human cases, outbreaks or unexpected health events are sometimes published in local newspapers (print or online) or reported by radio before being detected and reported by local health services	By monitoring the press and national and international television channels Email, applications for smartphones, social networks
International sources of information	Also used to identify events reported from a foreign country, even if they are not (yet) identified as being present domestically	International organizations and networks providing information on outbreaks, exposures and risks: WHO website, <sup>1</sup> CDC website, <sup>2</sup> ECDC website, <sup>3</sup> GISRS, <sup>4</sup> FAO website, <sup>5</sup> ProMED, <sup>6</sup> Google alert, etc.

<sup>1</sup> Disease outbreak news. Geneva: World Health Organization; 2018 ([www.who.int/csr/don](http://www.who.int/csr/don)).

<sup>2</sup> Centers for Disease Control and Prevention (CDC) website ([wwwnc.cdc.gov](http://wwwnc.cdc.gov)).

<sup>3</sup> European Centre for Disease Prevention and Control (ECDC): news and events ([www.ecdc.europa.eu/en/press/epidemiological\\_updates/Pages/epidemiological\\_updates.aspx](http://www.ecdc.europa.eu/en/press/epidemiological_updates/Pages/epidemiological_updates.aspx)).

<sup>4</sup> The Global Influenza Surveillance and Response System (GISRS) ([www.who.int/influenza/gisrs\\_laboratory](http://www.who.int/influenza/gisrs_laboratory)).

**Annex 8.** *Examples of event investigation and data collection forms*

**Event investigation form: source of report**

What is your name? .....

What is your phone number? .....

What is your position? .....

If report is second-hand information, what is the original source of information?  
(name, contact information)? .....

**Location of event (location where the event took place)**

What is the name of the village/district? .....

What is the name of the province? .....

**Description of the event**

Specify what you want to report (what happened/who is affected/what are the symptoms?)

.....

Number of cases among **children**: ..... Number of deaths among **children**: .....

Number of cases among **adults**: ..... Number of deaths among **adults**: .....

Number of cases among **males**: ..... Number of deaths among **males**: .....

Number of cases among **females**: ..... Number of deaths among **females**: .....

When did the problem **begin**? .....

Is the problem **ongoing**? YES  NO

What could be the cause of this event? .....

What are the main control measures being implemented? .....

What assistance do you need? .....

Is there any other information you wish to share? .....

**For office use only**

**ASSESSMENT** – If any of these conditions are met, a response is required.

Is the disease unusual/unexpected in this community? YES  NO

Could the disease have an impact on international travel or trade? YES  NO

Could the suspected disease cause outbreaks with high potential for spread (e.g. acute fever/illness: dengue, measles, etc.)? YES  NO

Is there a higher than expected mortality or morbidity from the suspected disease? YES  NO

Is there a cluster of cases or deaths with similar symptoms (e.g. fever, rash, arthralgia, haemorrhage and other symptoms)? YES  NO

Could the disease be caused by a bite from mosquitoes (e.g. signs of biting by mosquitoes)? YES  NO

Is there a suspected increase in the number of mosquitoes breeding in this area? YES  NO

If the event is a non-human event (e.g. increase in the number of mosquitoes), does the event have known or potential impact for human health? YES  NO

Date: .....

Name and signature of person completing this form: .....

.....

## Example of an event-based surveillance data reporting form

Date of this report	Date the report was submitted to the technical unit
Code	Write the code of the report in this format (YYYY-MM-number)
Report date and time	Write the date and time the health event was first reported to the technical unit
Verification date and time	Write the date and time the health event was confirmed/verified by the health staff
Health event	Write the type of health event reported
Location	Complete address (number, street, municipality, province) where the reported event was observed. For multiple locations, focus on description of cases
Start date	Date of start of event or date of onset of first case
Number of cases	Number of people affected
Description of cases	Who was affected (age and sex, nature of work)? What are the common signs and symptoms of cases? When, where?
Number of deaths	Initial number of reported deaths from the event
Description of deaths	Who was affected (age and sex), from where (address of fatalities)? When (dates of fatalities)? List the cause of death or include a description of symptoms prior to death
Laboratory examination	Indicate laboratory examinations carried out on specimens collected/tested
Is this an outbreak?	Yes or no
Who made the announcement?	Indicate type of report, e.g. press release, city ordinance creation
Was a report made?	Yes or no. If yes, was there an official report of the technical unit?
Assessment	Write the level of risk of this public health event (PHELC/PHERC/PHENC/PHEIC)
IHR notification decision questions	Please check what is applicable by consulting Annex 2 of the IHR document
Status of health event	Whether the health event is ongoing, controlled or closed
Actions taken	What was done? By whom? When?
Assistance needed	Specific assistance needed, if any
Event-based surveillance unit action	To just continue monitoring or will assistance be provided, etc?
Remarks	Important information not mentioned elsewhere
Who has been informed?	With whom has the information been shared (national and local health authorities, WHO and other stakeholders)
Sources of information	Name, office, designation and contact numbers of the person who gave the information
Prepared by	Name and signature of the technical unit staff/focal point who prepared the report, designation and contact details
Reviewed by	Name and signature of the supervisor who reviewed the report, designation and contact number/s
Noted by	Name and signature of the supervisor on duty and contact details
Approved by	Name and signature of Technical Unit Head, Division Chief, Director

IHR: International Health Regulations (2005).

PHELC/PHERC/PHENC/PHEIC: public health emergency of local/regional/national/international concern.

WHO: World Health Organization.

## **Annex 9.** *Operational priorities for entomological surveillance in the context of Zika virus*

### **Countries without *Aedes***

- Enhance surveillance of mosquitoes in border areas.
- Monitor imported goods (e.g. used tyres, plants) from countries endemic with/receptive to *Aedes*, using quarantine measures to avoid entry of invasive species of mosquitoes. Ovitrap traps can be used for this surveillance.
- Implement vector surveillance and control at points of entry – in accordance with the International health regulations (2005) – emphasizing nonchemical interventions such as source reduction.

### **Countries with *Aedes* but no evidence of Zika virus circulation**

- Establish sentinel surveillance of *Aedes* and collect data regularly. If any increase in *Aedes* density is detected, promptly target breeding sites with source reduction in a radius of 400 metres, and implement community awareness activities.
- Ensure placement of contingency stocks of nationally approved insecticides and equipment to respond to potential outbreaks of arboviruses.
- Develop adequate capacity, skills and equipment for control, and ensure availability of funds to respond to potential outbreaks of arboviruses.
- Identify local areas with high densities of *Aedes*.
- Prioritize the most productive breeding sites and target control measures.
- Aim for zero breeding sites in low-density areas and prevent expansion of the vectors to other areas by rapid control activities in the vicinity.
- Maintain constant monitoring of vector density through surveillance programmes. All efforts must be made to maintain vector density at a low level.

### **Countries with *Aedes* and evidence of Zika virus circulation**

- Establish sentinel surveillance of *Aedes* and collect data regularly. Surveillance data should reflect trends and impact of control measures.
- Develop adequate capacity, skills and equipment for control, and ensure availability of funds to manage the outbreak.
- Identify local areas with a high density of *Aedes*.
- Prioritize the most productive breeding sites and target control measures.
- Encourage community involvement to target smaller breeding sites in and around houses once a week.
- In the event of a large outbreak, enhance control to include targeted adult control measures such as fogging, along with larval control measures.
- Develop key messages for communication to the community. Target messages for schools and other community groups and organizations to support the campaign.



