1. Introduction

1.1 Background

The geographical distribution of Zika virus (ZIKV) has expanded globally, particularly since 2015 in the Americas. Since 2013, 31 countries and territories have reported cases of microcephaly and other central nervous system malformations associated with ZIKV infection, as of 17 February 2017. There are significant knowledge gaps around ZIKV and a lack of historical data on its vectors, transmission dynamics, and geographical distribution. Despite these challenges, there is a need to better describe the epidemiology of ZIKV transmission in a given place, at a given time in order to allow an assessment of the possibility of ZIKV infection for various populations, and to adapt public health recommendations accordingly for residents and travellers.

The proposed definitions in this interim guidance refine and replace those presented in the WHO interim guidance on surveillance for ZIKV infection, microcephaly and Guillain-Barré syndrome (7 April 2016). Further review of this guidance will take place to incorporate new understanding of ZIKV transmission.

1.2 Target audience

The primary audience for this guidance are public health authorities and policy-makers. The guidance can be used to categorize the presence of autochthonous vector-borne ZIKV transmission (not travel associated cases), and to adapt public health recommendations as appropriate. Classification of countries will be reviewed regularly to take into account changes in surveillance data.

1.3 Classification scheme

For the purposes of classification, 4 categories of ZIKV transmission were defined:

- Category 1. Area with new introduction or re-introduction with ongoing transmission
- Category 2. Area either with evidence of virus circulation before 2015 or area with ongoing transmission that is no longer in the new or re-introduction phase, but where there is no evidence of interruption
- Category 3. Area with interrupted transmission and with potential for future transmission
- Category 4: Area with established competent vector but no known documented past or current transmission

Some countries/territories/subnational areas are currently not at risk of ongoing vector-borne ZIKV transmission because of the absence of a competent vector and favourable climate, and are not included in this classification scheme.

For the purposes of classification, *Aedes aegypti* is considered the main competent vector of ZIKV because of it being the vector sustaining most Zika virus outbreaks. Other mosquito species could be added depending on new evidence for sustaining Zika virus transmission.

The epidemiology of ZIKV in affected countries will be reviewed on an ongoing basis.

2. Definitions

2.1 Surveillance reporting area

Characterization and categorization of vector-borne ZIKV transmission should be carried out at national and subnational levels when possible. Vector-borne ZIKV transmission is dependent on both vector presence and favourable climatic conditions, and the geographical distribution of ZIKV might mirror location of previous and/or current dengue outbreaks. The geographical area of the reporting unit should be of a size that allows for meaningful characterization of the transmission dynamic. The area of surveillance should also reflect the area where ZIKV transmission may occur based on the presence of the virus, competent vectors, climatic and geographical conditions, or evidence of dengue transmission, rather than administrative boundaries.

2.2 Definitions of categories

The categories are the following.

**Category 1. Area with new introduction or re-introduction with ongoing transmission**
a. A laboratory-confirmed, autochthonous, vector-borne case of ZIKV infection in a country/territory/subnational area where there is no evidence of virus circulation before 2015, whether it is detected and reported by the country/territory/subnational area where infection occurred, or by another country by diagnosis of a returning traveller; or

b. A laboratory-confirmed, autochthonous, vector-borne case of ZIKV infection in a country/territory/subnational area where transmission has been previously interrupted, whether it is detected and reported by the country where infection occurred, or by another country by diagnosis of a returning traveller.

If a case due to vector-borne transmission occurs in a country/territory/subnational area where there is no evidence of ZIKV circulation prior to 2015, for classification of the area in this category the case must be in an area where A. aegypti, a vector that can support ongoing virus transmission, is established. Any limited transmission in a country where the vector A. albopictus alone is present, will not result in the inclusion of that country in Category 1, until further field evidence of involvement of this vector in sustainable ZIKV transmission.

It is anticipated that any country classified as Category 1 will ultimately be reclassified as either Category 2 or Category 3.

Category 2. Area either with evidence of virus circulation before 2015 or area with ongoing transmission that is no longer in the new or re-introduction phase, but where there is no evidence of interruption

This category takes into account those countries with known historical laboratory evidence of ZIKV circulation prior to 2015, based on the literature as well as all ZIKV surveillance data whether detected and reported by the country where infection occurred or by another country reporting a confirmed case in a returning traveller.

Countries in this category may have seasonal variations in transmission. In some countries, there may be regular occurrence of cases; in others, transmission may be low level with less frequent, or sporadic, occurrence of cases. These countries may also experience outbreaks of ZIKV disease. Over time, Category 1 countries will likely transition to Category 2.

The timeline for determining the transition of a country from Category 1 to Category 2 is currently unknown, but based on epidemic patterns from introduction of other arboviruses, it is likely to be approximately 2 years after ZIKV was newly or re-introduced.

Laboratory criteria to ascertain the presence of ZIKV in past studies are:

- Detection of the virus in humans, mosquitoes or animals; and/or
- Serologic confirmation of ZIKV infection with tests conducted after 1980, and considered as confirmed infection on expert review based on testing for all appropriate cross-reactive flaviviruses and utilization of comprehensive testing methodologies. Because of testing and interpretation limitations with serological data antedating 1980, they were not used for classification purposes.

Over time, countries in this category may experience outbreaks of disease which will be difficult to distinguish from seasonal fluctuations or from surveillance artefacts. The following criteria may be useful to characterise an outbreak in such settings: an increase of the incidence of laboratory confirmed, autochthonous, vector-borne ZIKV infections more than 2 standard deviations above the baseline rate, or a doubling of cases over a 4 week period.

Data collection and analysis should be enhanced to monitor the geographical distribution and temporal trends of transmission, thereby establishing an incidence pattern. Indicators such as detection of travel-associated cases or ZIKV complications may be used to demonstrate circulation of the virus or indicate the epidemiology of transmission.

It is possible that a country classified as Category 2 can be reclassified as Category 3.

Category 3. Area with interrupted transmission and with potential for future transmission

Some countries – particularly those that are geographically isolated and have small populations – may be classified as countries where transmission has been interrupted (Category 3). Historical evidence exists that, in some instances, such as in Yap (the Federated States of Micronesia) or French Polynesia, ZIKV transmission may be interrupted after first introduction; however, the potential for re-introduction remains.

Criteria for possible interruption include geographic isolation of populations as occurs on small islands, temperate climate, and/or successful ongoing surveillance and control activities. It is likely that in such settings a Zika event will appear as a focal outbreak and disease transmission will not span the seasons.

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1 Autochthonous infection is considered to be an infection acquired in-country, i.e. among patients with no history of travel during the incubation period or who have travelled exclusively to non-affected areas during the incubation period.

2 Other information should be analysed to support the assessment of pattern of transmission, such as: when available, ZIKV surveillance data in previous year(s) (including notification of Zika disease cases, ZIKV associated complications and sero-surveys); transmission season of dengue; climate pattern and vector surveillance data.
The minimum timeline for determining transition to an interrupted state is 12 months after the last confirmed case, and no cases identified in travellers. For countries with a high capacity for diagnostic testing, consistent timely reporting of diagnostic results, a comprehensive arboviral surveillance system and/or a temperate climate or island setting, the interruption of vector-borne transmission is defined as the absence of ZIKV infection 3 months after the last confirmed case.

Countries where interruption is epidemiologically likely to have occurred should provide surveillance data to WHO to support the assessment by expert review.

Laboratory surveillance should be strengthened to provide sufficient evidence that transmission has ended. Evidence includes negative results from molecular tests on samples taken from patients with suspected ZIKV infection – for example during investigations of clusters of febrile illness or an itchy rash of unknown origin, or on samples taken as part of clinical diagnosis or arbovirus surveillance activities.

Countries/territories/subnational areas in this category may have a new introduction and experience a new outbreak and will thus be reclassified as Category 1.

**Category 4. Area with established vector but no documented past or current transmission**

Category 4 includes all countries/territories/subnational areas where the main competent vector (*A. aegypti*) is established, but which have not had a documented, autochthonous, vector-borne case of ZIKV infection.

This category also includes a subgroup of countries/territories/subnational areas where ZIKV transmission may occur because of a shared border with a neighbouring Category 2 country, by belonging to the same ecological zone and having evidence of dengue virus transmission.

In this subgroup, a first laboratory-confirmed, autochthonous vector-borne case of ZIKV infection may not necessarily indicate new introduction (Category 1), but rather previously unknown and undetected transmission (Category 2), and these countries/territories/subnational areas will be reclassified accordingly. Given the high potential for ZIKV transmission, countries in this category are encouraged to enhance surveillance to investigate the possibility of undetected circulation; if confirmed, surveillance should be continued to better understand the geographical distribution and temporal trends of transmission.

### 3. Guidance development

#### 3.1 Acknowledgements

This document has been developed with new evidence and knowledge appearing from surveillance data by a guideline development group composed of the following individuals:

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#### 3.2 Guidance of development methods

The document was produced following a face-to-face meeting of the guidance development group and on review of the surveillance data. Consensus on the recommendations was reached through group discussion.

#### 3.3 Declaration of interests

All external contributors completed the standard WHO Declaration of Interests (DOI) form. The forms were reviewed by WHO staff and managed in accordance with WHO guidelines on a case-by-case basis. No competing interests were identified from the external contributors,
precluding participation in the guideline development process.

3.4 Review date

This guidance was produced under emergency procedures and will remain valid until December 2017, unless revised earlier. Triggers for an earlier revision include new knowledge on competent vectors, vector distribution or transmission mode.