



## RAPID RISK ASSESSMENT

# Outbreak of yellow fever in Brazil

Third update, 16 March 2018

## Conclusions

In September 2017, the Ministry of Health in Brazil declared the end of the 2016–2017 yellow fever outbreak in the country. The upsurge of human cases since December 2017 and the continuous non-human primate epizootics since September 2017 indicate a continued or resumed increase in yellow fever virus circulation in Brazil. Since January 2018, most of the yellow fever cases have been reported from São Paulo, Rio de Janeiro and Minas Gerais states.

To date, an urban cycle of yellow fever transmission by *Aedes aegypti* (or *Aedes albopictus*) has not been documented in Brazil. However, the detection of non-human primate cases in the vicinity of the metropolitan regions of São Paulo and Rio de Janeiro remains of concern, especially in areas with suboptimal vaccination coverage. This is particularly relevant for municipalities that were previously not considered at risk for yellow fever and where routine yellow fever vaccination was not indicated. Therefore, the possibility of an urban cycle of yellow fever transmission remains.

Since January 2018, Brazilian national health authorities have been intensifying and extending vaccination activities through mass yellow fever vaccination campaigns in Rio de Janeiro and São Paulo states. Additional vaccination campaigns have been conducted in Bahia State since February 2018. The overall target population was around 22.7 million people. According to the Brazilian authorities, as of 13 March 2018, preliminary results of the mass yellow fever vaccination campaign indicate that 17.5 million people have been vaccinated.

The risk of yellow fever importation and subsequent transmission in continental Europe is currently very low because the risk of the virus being introduced by viraemic travellers into an area with established, competent and active mosquito vector population is very low.

## Options for response

### Advice to travellers

EU/EEA citizens who travel to, or live in areas at risk of yellow fever in Brazil and other countries in South America are advised to:

- Check their vaccination status and get vaccinated if necessary, in accordance with national and WHO recommendations. Vaccination against yellow fever is recommended by WHO for people visiting or living in yellow fever risk areas, from nine months of age and without contraindications [1-3]. An individual risk-benefit analysis should be conducted by professionals in tropical or travel medicine centres prior to vaccination, taking into account the period, destination, duration of travel and likelihood of being bitten by mosquitoes as well as individual risk factors for adverse events following yellow fever vaccination.

- Take measures to prevent mosquito bites indoors and outdoors, especially between sunrise and sunset when mosquito vectors are most active. This also apply to places such as large recreational areas and parks, botanical gardens and natural reserves. The measures include:
  - the use of mosquito repellent in accordance with the instructions indicated on the product label;
  - wearing long-sleeved shirts and long trousers;
  - sleeping or resting in screened/air-conditioned rooms or using mosquito nets at night and during the day.

International travellers returning from affected areas may be requested to show proof of yellow fever vaccination (or a contraindication certificate) when entering countries or territories infested with *Aedes aegypti* mosquitoes.

Vaccination requirements and recommendations for international travellers are available from the World Health Organization's website [2,4-10].

## Advice to health professionals

Physicians, health professionals and travel health clinics should be provided with, or have access to regularly [updated information on areas with ongoing yellow fever transmission](#) and should consider yellow fever in the differential diagnoses for illnesses in unvaccinated travellers returning from at-risk areas. To reduce the risk of adverse events following immunisation, healthcare practitioners responsible for yellow fever vaccinations should be aware of the contraindications and follow the manufacturers' advice on precautions before administering yellow fever vaccine [3,11].

## Option for EU Overseas Countries and Territories and Outermost Regions with presence of *Aedes aegypti*

In the EU Overseas Countries and Territories and EU Outermost Regions where *Aedes aegypti* is established or has been introduced, verification of yellow fever vaccination status should be considered for travellers coming from Brazil in order to reduce the risk of yellow fever importation and subsequent spread.

## Options for the safety of substances of human origin (SoHO)

The risks and options for the safety of substances of human origin (SoHO) remain the same as in the [second updated ECDC rapid risk assessment](#), published on 18 January 2018 [12].

## Source and date of request

ECDC internal decision, 8 March 2018.

## Public health issue

This is the third update of a rapid risk assessment originally produced on [25 January 2017](#) and updated on [13 April 2017](#) and [18 January 2018](#) [12-14]. The third update assesses the risk to EU/EEA countries and citizens associated with the ongoing outbreak of yellow fever in Brazil. The update of the rapid risk assessment was triggered by the evolution of the epidemic in Brazil and reports of travel-associated yellow fever cases with exposure in Brazil returning to Europe.

## Consulted experts

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## Disease background information

Background information on the yellow fever can be found on the ECDC website: [Facts about yellow fever](#).

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\* Experts from WHO reviewed this risk assessment, however the views expressed in this document do not necessarily represent the views of WHO.

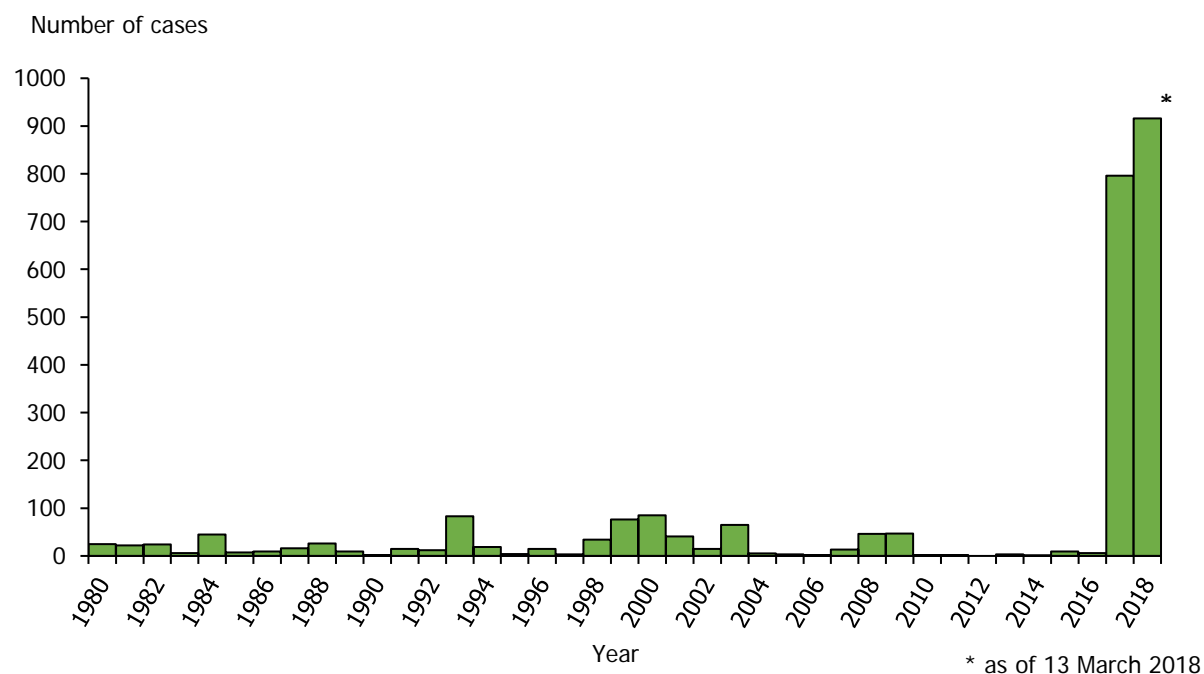
## Event background information

### Epidemiological background of yellow fever in Brazil

In the Americas, yellow fever virus transmission is maintained through a sylvatic cycle involving non-human primates and forest-canopy mosquitoes of two genera, *Haemagogus* and *Sabethes*. Humans can be infected after being bitten by yellow-fever-infected mosquitoes when they residing close to or entering forest areas. In Brazil, this cycle occurs in a large part of the country, such as the forest ecosystem in the basins of the Amazon, Rios Araguaia-Tocantins and Paraná [15]. Yellow fever has a cyclical pattern in forested areas of South America, with alternating epidemic and endemic periods, as seen in Brazil (Figure 1) [16].

Prior to the 2016–2017 outbreak, the last epidemic occurred between 2007 and 2009 [17]. The case fatality rate during the period 1980 to 2016 was 52%. Occurrence of yellow fever cases in Brazil follows a seasonal pattern, with the majority of the cases detected between January and June during the 2000–2012 period [15]. In South America, the report of epizootics in non-human primates (e.g. sudden die-offs of New World monkeys) supports a sustained virus circulation in favourable ecosystems. The latter event is considered as a sentinel event indicating an increased probability of transmission of sylvatic origin to humans. Therefore, such events are under surveillance in Brazil and are used to define the priority areas for disease prevention and control [15,16,18].

**Figure 1. Distribution of confirmed human cases of yellow fever by year, Brazil, 1980 – 13 March 2018**



Source: Adapted from Ministry of Health, Brazil [19]

An urban transmission cycle can be established when viraemic travellers are bitten by *Aedes aegypti* mosquitoes upon return to urbanised areas. The urban transmission of yellow fever has the propensity to amplify and spread rapidly in human populations with low vaccination coverage. *Aedes aegypti* is present in all Brazilian states [20,21]. The season for the highest mosquito vector activity lasts from December to July in the southern part of Brazil. Since the outbreak of urban yellow fever in Acre in 1942, Brazil has only reported sylvatic yellow fever cases [22]. *Aedes albopictus*, a species for which competency was demonstrated during laboratory experiments, is established in most parts of the country [20,23].

### Outbreak of yellow fever in Brazil

From July 2016 to June 2017, 779 human cases of yellow fever and 262 deaths were reported [24]. Between July 2017 and 13 March 2018, the Brazilian health authorities reported 920 laboratory-confirmed human cases of yellow fever, including 300 deaths (CFR 33%). The cases occurred in São Paulo (376), Minas Gerais (415), Rio de Janeiro (123), Espírito Santo (5) and Distrito Federal (1) [19]. The probable place of infection for all confirmed human cases were areas with previously documented cases in non-human primates, with the exception of the case in Distrito Federal. Between July 2017 and 13 March 2018, 617 confirmed epizootics were detected in non-human primates [19]. Of these, 502 were reported in São Paulo State, 81 in Minas Gerais, 30 in Rio de Janeiro State, two in Tocantins and one each in Mato Grosso and Espírito Santo. The reports of the detections include epizootics in non-human primates in the vicinity of the metropolitan regions of São Paulo and Rio de Janeiro [19,25].

Entomological investigations conducted during the 2016–2017 outbreak in some of the affected states isolated *Haemagogus* mosquitoes positive for yellow fever virus, but no evidence of transmission by *Aedes aegypti* was found [26].

In January 2018, the health authorities in Brazil reported that yellow fever virus had been detected in *Aedes albopictus* mosquitoes captured in rural areas of Ituêta and Alvarenga municipalities in Minas Gerais State in 2017 [27,28]. Further investigation is needed to determine the significance of this finding to confirm vector competence and vector capacity in transmitting yellow fever [27,28].

## Travel data and travel-associated cases

Since the beginning of January 2018 and as of 9 March 2018, five travel-associated cases of yellow fever have been identified among unvaccinated EU/EEA travellers to Brazil – in Romania (1), France (one confirmed and one suspected), the United Kingdom (one) and the Netherlands (one) [29-32]. Additionally, Switzerland detected a case in an unvaccinated traveller who died [30,33]. All cases visited areas in Brazil considered at-risk for yellow fever as described in the international travel health recommendations, notably Rio de Janeiro coastal area (Rio de Janeiro city or Ilha Grande) [2,32].

Outside of Europe, three Chilean citizens (all three cases confirmed) and three Argentinians contracted yellow fever while visiting Brazil (state of Rio de Janeiro, São Paulo or Minas Gerais) in the first two months of 2018 [27,34,35]. Of the three Chileans, two died. According to WHO, two of the Argentinian citizens were likely to have been exposed in Ilha Grande, part of the coastal municipality of Angra do Reis (state of Rio de Janeiro) or in Ilhabela located in the neighbouring Metropolitan Region of Vale do Paraíba e Litoral Norte (state of São Paulo). Three of the Chilean citizens were probably exposed in the municipality of Angra do Reis in the state of Rio de Janeiro.

## Yellow fever vaccination

Countries with a risk of yellow fever transmission and countries requiring yellow fever vaccination are listed on the WHO International Travel and Health website [1]. Yellow fever vaccination is not recommended universally in Brazil (see [latest WHO map](#)) [2]. WHO recommends vaccination of all unvaccinated travellers aged over nine months and without contraindication who are travelling to at-risk areas [3]. Vaccination should be obtained at least ten days prior to travel [3].






On 16 January 2018, WHO revised the areas at risk of yellow fever transmission and included the entire state of São Paulo in the list. Consequently, vaccination is recommended for travellers visiting any area in the state of São Paulo [1]. Individuals residing or travelling to areas at risk who cannot be vaccinated because they do not meet the vaccination criteria are of particular concern (e.g. babies under nine months of age and people with underlying health conditions). These individuals should apply strict personal protection measures to prevent mosquito bites [3].

The vaccination campaigns in Brazil started in January 2018 and are still ongoing in São Paulo, Bahia and Rio de Janeiro states. As of 13 March 2018, 17.5 million people had been vaccinated. The vaccination coverages are 69%, 95% and 54% in Rio de Janeiro, São Paulo and Bahia, respectively [19].

**Figure 2. Distribution of confirmed yellow fever cases by state, Brazil, July 2017–6 March 2018**



Confirmed cases of locally-acquired yellow fever, as of 06 March 2018

-  States with confirmed locally-acquired cases since July 2017
-  Area at risk for yellow fever transmission
-  Area considered at no risk for yellow fever transmission
-  Federal state
-  Probable place of infection–European travellers



ECDC. Map produced on: 08 Mar 2018  
 ECDC map maker: <https://emma.ecdc.europa.eu>

Source: Adapted from WHO yellow fever vaccination recommendations in the Americas, 2018 [2]

## ECDC threat assessment for the EU

### Yellow fever risk in Brazil

Since January 2017, Brazil has been experiencing an increased circulation of yellow fever, substantiated by an increase in epizootics among non-human primates. A first related upsurge in human cases of yellow fever occurred between January and May 2017. This first epidemic predominantly affected the eastern part of Minas Gerais state and Espírito Santo state [36].

Following this epidemic and during the austral winter months of 2017 (June to December 2017) considered as unfavourable for epizootic yellow fever virus transmission, an unusually high number of epizootics occurred in the northern part of São Paulo state. This pattern supports a continued viral circulation among non-human primates in forested areas of São Paulo state.

Since December 2017, a second outbreak has affected mainly three states: Minas Gerais, Rio de Janeiro and São Paulo. As of 6 March, the number of human cases in 2018 has exceeded the cumulative number for the whole of 2017 and the outbreak reached the areas surrounding major Brazilian metropolitan areas (São Paulo and Rio de Janeiro).

The second outbreak raises concerns about the potential emergence of an urban cycle of yellow fever due to its proximity to areas with high population density, especially in areas not considered at risk prior to 2017. Indeed, São Paulo city has been considered at risk since January 2018 and Rio de Janeiro city since April 2017 [1]. So far, there is no evidence of an urban cycle of yellow fever involving urban vectors (*Aedes aegypti* or *Aedes albopictus*) in the metropolitan areas of São Paulo and Rio de Janeiro [19,25,27,37].

Nevertheless, the continuous reports of epizootics in non-human primates in the vicinity of the metropolitan regions of São Paulo and Rio de Janeiro and sporadic human cases in suburban areas increase the possibility of peri-urban or urban cycles of yellow fever transmission becoming established in areas with competent vectors [23,38].

This unusual situation has led the Brazilian health authorities to launch mass yellow fever vaccination campaigns since January 2018 [19].

### Yellow fever risk for EU/EEA citizens travelling to/residing in affected areas

Travellers visiting affected areas and residents living in affected areas are at risk of infection if they have not been vaccinated.

Reports of six cases of yellow fever (five confirmed and one suspected) identified over the past three months among unvaccinated European travellers to areas in Brazil considered at risk for yellow fever transmission highlight the need to follow WHO recommendations. This is particularly relevant for international travellers to areas in Brazil deemed to be at risk where the exposure has increased.

By comparison, there were six travel-related cases of yellow fever among EU/EEA travellers between 1999 and 2016 [12]. Two additional travel-related yellow fever cases were reported in 2017: one in January 2017 in a Danish citizen who travelled to Bolivia and one in March 2017 in a traveller returning from Suriname to the Netherlands [12].

This recent increase in the number of travel-related cases among unvaccinated travellers highlights the fact that despite the national and international vaccination recommendations, travellers visiting at risk areas in Brazil are not systematically ensuring that they get vaccinated. Given the high volume of EU/EEA travellers to Brazil, more cases among unvaccinated EU/EEA travellers may be expected in the coming months.

### Risk of transmission in continental EU/EEA

Importation of yellow fever remains possible through infected returning travellers, as demonstrated recently with six yellow fever cases among European travellers. The establishment of an urban cycle of yellow fever transmission in Rio de Janeiro or São Paulo would significantly increase the number of exposed travellers and the likelihood of importation to European countries.

The probability of local yellow fever transmission in the EU/EEA following introduction by a viraemic traveller is currently considered very low as weather conditions during the winter season in continental Europe are not favourable to vector activity. Recent studies conducted in France have shown that *Aedes albopictus* mosquitoes collected in southern France can transmit yellow fever virus in laboratory settings [39]. To date yellow fever transmission via *Aedes albopictus* has not been observed in nature.

## Risk of transmission in the EU overseas countries and territories (OCT) and outermost regions (OMR)

French Guiana is enzootic for yellow fever. The most recent locally-acquired human case was identified in 2017 in a person who was most likely infected in the border region of French Guiana and Brazil [40]. Yellow fever vaccination has been mandatory for residents since 1967 and is compulsory for people entering French Guiana. Vaccination coverage through routine vaccination is high and was estimated at 95.9% (95% CI 95.5–96.3) in 2009 [41].

*Aedes aegypti* is established in the British, French and Dutch OCTs and OMRs of the Caribbean region and in the Portuguese OMR of Madeira. Recently, *Aedes aegypti* has been detected in the Spanish OMR of Fuerteventura (Canary Islands), as notified by the Spanish public health authorities through the Early Warning Response System [42]. In the northern hemisphere (e.g. in Madeira) vector activity is currently low. However, the risk may increase towards the summer months.

The French High Council for Public Health has published guidelines for reducing the risk of importing yellow fever into receptive areas (where *Aedes aegypti* is present). Recommendations include:

- vaccination of travellers to risk areas;
- integrated vector management;
- enhancement of clinicians' awareness to facilitate early detection of suspected cases.

## Yellow fever and safety in substances of human origin (SoHO)

Transmission of yellow fever through transfusion or transplantation has never been reported although a risk of infectious SoHO donations from an unvaccinated asymptomatic viraemic donor cannot be excluded. The yellow fever attenuated virus from the 17D vaccine has been transmitted through transfusion of blood donated by recently immunised donors [43]. Donation of blood is possible four weeks after vaccination with attenuated viral vaccine [44].

For organs, tissues and cells, the risk of yellow fever transmission from a donor who may have visited an affected area should be balanced with the likelihood of virus transmission. If an organ donor was vaccinated against yellow fever during the four weeks before donation, an individual risk assessment of the immune status of all prospective recipients is mandatory. Yellow fever vaccination is contraindicated for immunocompromised patients after solid organ and haematopoietic stem cell transplantation. Potential transplant patients living in countries endemic for yellow fever or planning travel to endemic countries should be immunised before transplantation.

## Disclaimer

ECDC issued this risk assessment document on the basis of an internal decision in accordance with Article 10 of Decision No 1082/13/EC and Article 7(1) of Regulation (EC) No 851/2004 establishing a European centre for disease prevention and control. In the framework of ECDC's mandate, the specific purpose of an ECDC risk assessment is to present different options on a certain matter with their respective advantages and disadvantages. The responsibility on the choice of which option to pursue and which actions to take, including the adoption of mandatory rules or guidelines, lies exclusively with the EU/EEA Member States. In its activities, ECDC strives to ensure its independence, high scientific quality, transparency and efficiency.

This report was written under the coordination of an Internal Response Team (IRT) at the European Centre for Disease Prevention and Control (ECDC). All data published in this risk assessment are correct to the best of our knowledge on 15 March 2018. Maps and figures published do not represent a statement on the part of ECDC or its partners on the legal or border status of the countries and territories shown.

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