

RAPID RISK ASSESSMENT

Outbreaks of yellow fever in Angola, Democratic Republic of Congo and Uganda

First update, 27 May 2016

Main conclusions and options for response

In the EU/EEA, the risk of yellow fever virus being introduced is limited to unvaccinated viraemic travellers coming from epidemic areas. Given that outbreaks of yellow fever in urban settings have the potential for rapid spread and that significant yellow fever epidemics are ongoing in Angola, DRC and Uganda, EU/EEA Member States should consider a range of options for response.

Information for travellers to and EU citizens residing in areas with active transmission

Travellers visiting countries where there is evidence of persistent or periodic yellow fever virus transmission and EU citizens residing in these countries should:

- Be made aware of the risk of yellow fever;
- Check their vaccination status and get vaccinated. Vaccination against yellow fever is recommended for all those ≥9 months old travelling to areas where there is evidence of persistent or periodic yellow fever virus transmission. WHO publishes a list of countries, territories and areas with yellow fever vaccination requirements and recommendations [1] which includes Angola, Democratic Republic of Congo and Uganda. In Angola, the country requirement specifies that a yellow fever vaccination certificate is required for travellers aged over nine months. To reduce the risk of serious adverse events, healthcare practitioners should be aware of the contraindications and follow the manufacturers' advice on precautions to take before administering yellow fever vaccine [2].
- Take measures to prevent mosquito bites indoors and outdoors, especially between sunrise and sunset when *Aedes* mosquito vectors are most active and biting. These measures include:
 - The use of mosquito repellent in accordance with the instructions indicated on the product label.
 - Wearing long-sleeved shirts and long trousers, especially during the hours when the type of mosquito known to transmit the yellow fever virus (*Aedes*) is most active.
 - Sleeping or resting in screened or air-conditioned rooms or using mosquito nets, at night and during the day.

Options to prevent importation into EU/EEA countries

Implement the WHO International Health Regulations (IHR) Emergency Committee recommendation to only allow travellers showing proof of a valid vaccination record for yellow fever to leave Angola. The procedure should also be applied to land and sea borders. Entry screening in the EU, for proof of vaccination, would be of

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limited value because of the limited availability of direct flights and the high likelihood of indirect travel routes into the EU.

• Alternatively, EU Member States, particularly those including areas with established populations of suitable *Aedes* mosquitoes, could prevent the arrival of viraemic travellers by requesting proof of valid vaccination when issuing a visa.

Options to prevent transmission in EU/EEA countries

- Raise awareness of public health stakeholders, in particular clinicians and travel health clinics, concerning the risk of yellow fever virus introduction into the EU through unvaccinated viraemic travellers coming from epidemic areas.
- Clinicians should consider yellow fever among differential diagnoses for travellers returning from affected areas.
- Ensure that clinicians and travel health clinics get updated information about areas with an ongoing yellow fever outbreak to support their diagnosis in travellers returning from those areas.
- Apply strict personal prevention measures against *Aedes* mosquito bites for any suspected and confirmed yellow fever cases through the use of a mosquito net in receptive areas for yellow fever transmission (i.e. areas with active competent vectors and human populations susceptible to yellow fever infection).
- Implement focal vector control in the areas where unvaccinated viraemic travellers have stayed. This option helps to reduce the risk of onward autochthonous transmission to the EU/EEA mainland and EU Overseas Countries and Territories (OCT) and Outermost Regions (OMR), in areas where yellow fever vectors are present. The vector competence of European *Aedes albopictus* mosquito populations needs to be assessed.

Source and date of request

ECDC internal decision, 17 May 2016

Public health issue

This document assesses the risk of yellow fever infections in EU/EEA countries related to the ongoing outbreak of yellow fever in Angola, DRC and Uganda.

ECDC published a rapid risk assessment on 25 March 2016.

Consulted experts

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ECDC acknowledges the valuable contributions of all experts. Although experts from the World Health Organization (WHO) reviewed the risk assessment, the views expressed in this document do not necessarily represent the views of WHO. All experts have submitted declarations of interest and a review of these declarations did not reveal any conflicts of interest.

Some of the data used in this rapid risk assessment were collected during a mission to Angola in May 2016.

Disease background information

Yellow fever is an acute viral haemorrhagic vector-borne disease affecting humans and non-human primates in 34 countries across sub-Saharan Africa and in tropical areas of 13 countries across South and Central America, from Panama to the northern part of Argentina [1,2]. Autochthonous transmission of yellow fever has never been detected in Asia, although the competent vector is present in south and south eastern areas of the continent [5].

Yellow fever is caused by a virus of the *Flavivirus* genus of the *Flaviviridae* family and transmitted by infectious mosquitoes of *Aedes* and *Haemagogus* genera. Monkeys and humans act as amplifying hosts. The virus originated in Africa and was introduced to the Americas several hundred years ago.

In Africa, there are three cycles of yellow fever transmission:

- 1. The sylvatic cycle, in the forest, where the presence of the virus is maintained through transmission among non-human primates by several species of sylvatic *Aedes* mosquitoes. Infected mosquitoes that bite humans entering the forest cause sporadic cases of yellow fever.
- 2. Intermediate or rural cycle, at the margins of the forest and in the savannah, which are zones of emergence of the virus, where the disease is transmitted by sylvatic *Aedes* mosquito and *Aedes aegypti*.
- 3. Urban cycle, when an infected human, returning to urban areas where the highly effective and anthropophilic *Aedes aegypti* vector is present, initiates human-to-human transmission cycles. Large epidemics, with tens of thousands of deaths, have been recorded in Africa.

The competence of *Aedes albopictus* for the transmission of the yellow fever virus has been demonstrated in Brazil using a Brazilian strain of yellow fever virus. In this study the dissemination and infection rates were lower than those observed for *Aedes aegypti*. However, the ability of *Aedes albopictus* to transmit the yellow fever virus cannot be ruled out in areas where infestation and biting indexes are high, even though its role in yellow fever outbreaks has not been demonstrated [4-8].

The annual number of yellow fever cases reported to WHO is presented in Figure 1 [11]. Between 1987 and 1991, recurrent yellow fever outbreaks were notified in Nigeria with more than 17 000 cases. In 2011, a large epidemic took place in Burkina Faso, Nigeria and Sierra Leone. Two previous outbreaks of yellow fever have been documented in Angola: one in 1971 (65 cases) and the other in 1988 (37 cases).





Data source: 1974-2014 from WHO Global Health Observatory data repository

The number of reported cases is commonly underestimated. A study published in 2014 estimated that 130 000 (95% CI 51 000–380 000) severe cases and 78 000 (95% CI 19 000–180 000) deaths due to yellow fever had occurred in Africa in 2013, accounting for about 90% of the global number of cases [10].

In the past two decades imported cases of yellow fever have been reported in Europe among unvaccinated travellers returning from Ivory Coast (Germany, 1999), Gambia (Belgium, 2001) and Ghana (Spain, 2009) [11,12].

Up to 85% of infections in humans are either asymptomatic or only result in mild illness [15]. After an incubation period of typically three to six days, infection occurs in one or two phases [4]. The initial symptoms include sudden onset of fever, chills, severe headache, back pain, general body aches, nausea, vomiting, fatigue and weakness [15]. Most people improve after the first phase but after a brief remission around 15 to 25% of cases develop the severe form of the disease, characterised by high fever and jaundice, and in some cases bleeding, eventually resulting in a shock and multiple organ failure. Up to 50% of severe cases may die. There is no specific treatment for yellow fever [16]. Infection provides life-long immunity.

Yellow fever infection is challenging to diagnose, especially during the early stages. Differential diagnoses for yellow fever include: malaria, haemorrhagic fevers (e.g. dengue haemorrhagic fever, Lassa fever, and Crimean-Congo haemorrhagic fever), leptospirosis, viral hepatitis and liver failure (e.g. toxic hepatitis).

The virus can be detected in blood specimens by RT-PCR, antigen-capture or viral isolation. For primary arbovirus infections, a serological diagnosis can be made by detecting specific IgM antibodies one week after infection (for secondary arbovirus infections, IgM and IgG need to be detected) [15].

Prevention and outbreak control

Yellow fever is effectively prevented through vaccination with the live attenuated vaccine [4].

Mass vaccination campaigns are the most effective public health strategy to control yellow fever outbreaks. A global vaccine stockpile is managed by the International Coordinating Group (ICG) on Vaccine Provision, which functions as a revolving fund for epidemic response [16]. In the long term, introducing preventive immunisation through routine childhood vaccination in endemic countries can significantly reduce the burden of the disease.

Yellow fever vaccination is recommended for travellers ≥ 9 months old to areas where there is evidence of persistent or periodic yellow fever virus transmission [1]. The vaccine is recommended to protect individual travellers at risk of exposure to yellow fever and to prevent international spread of the disease from endemic countries to countries with competent vectors [1]. Some adverse effects associated with the vaccine have been reported and a case-by-case assessment of the risks and benefits of yellow fever vaccination should be considered for some risk groups, such as older people or those with underlying health conditions [17]. According to WHO 'when considering vaccination, any traveller must take into account the risk of being infected with yellow fever virus, country entry requirements, as well as individual risk factors (e.g. age, immune status) for serious vaccine-associated adverse events' [1]. To reduce the risk of serious adverse events, healthcare providers should be aware of the contra-indications and follow the manufacturer's guidance on the precautions to be considered before administering yellow fever vaccine [2]. Complementary preventive measures, especially for travellers, include using insect repellent and wearing protective clothing.

The period of protection provided by yellow fever vaccination, and the term of validity of the certificate has been changed from 10 years to life, in accordance with a Word Health Assembly resolution, and this should come into effect from July 2016. On 19 May 2016, the Emergency Committee of the International Health Regulations (2005) advised for immediate application of the policy of one lifetime dose of yellow fever vaccine in light of the limited worldwide vaccine supply [20].

Mosquito control contributes to prevention of yellow fever outbreaks and is critical in situations where vaccination coverage is low or the vaccine is not immediately available. Mosquito control includes killing adult mosquitoes and larvae by using insecticides and larvicides, as well as eliminating mosquito breeding sites. Community involvement through activities, such as cleaning household drains and covering water containers where mosquitoes can breed, is a very important and effective way to control mosquitoes, but requires some time for preparation and implementation [4,21].

Possible shortage of yellow fever vaccine has been a concern for several years. According to the latest update from UNICEF dated May 2016, *during 2015, UNICEF increased total aggregate awards to suppliers to reach approximately 98 million doses for 2016–2017. However, whereas supply can meet emergency stockpile and routine requirements, it is insufficient to meet all preventive campaign demands, which increased the total demand through UNICEF to 109 million doses* [22]. According to Lucey and Gostin, a vaccine shortage can be anticipated if yellow fever spreads to other countries or regions, especially if large urban populations are to benefit from mass vaccination campaigns [23].

Event background information

Situation in Angola

On 21 of January 2016, WHO was notified by the IHR focal point in Angola of an ongoing yellow fever outbreak. The first cases reported were two males living in the municipality of Viana, a densely populated municipality on the outskirts of Luanda. The first case presented with yellow fever symptoms to a private clinic on 5 December 2015 [24]. In the following months, suspected cases were reported in all 18 provinces of Angola and confirmed cases were reported in 14 provinces.

Yellow fever infection was initially confirmed in three patients by PCR at the Zoonosis and Emerging Disease Laboratory of the National Institute for Communicable Diseases in Johannesburg, South Africa in early January and then at the Pasteur Institute in Dakar, Senegal on 20 January 2016. Following the confirmation of yellow fever infection cases in Luanda province and other provinces of Angola, the national reporting system was enhanced to collect epidemiological information on suspected cases and samples for laboratory confirmation.

From 21 January to 22 May 2016, the Angolan Ministry of Health notified 2 536 yellow fever cases, of which 747 were confirmed and 301 fatal (case fatality ratio: 11.9%), 88 of these being among confirmed cases (CFR: 11.8%).

The epidemic curve (Figure 2) shows that the highest number of suspected and confirmed cases was reported in February and March 2016, with a peak of notification of more than 80 confirmed cases reported per week at the end of February. Since April, the number of new cases has declined in Angola and in the two most affected

provinces of Luanda and Huambo it has decreased to an average of 30 cases per week. However, transmission of yellow fever has continued to spread to new areas and has increased in Benguela province.





Data source: [25]

Note: Data from greyed columns is incomplete due to reporting delays

The epidemic curve should be interpreted with caution because it is likely that a significant proportion of cases has not been diagnosed and reported, particularly during the early stages of the epidemic. Furthermore, the epicurve presents cases by week of onset, therefore the number of cases presented for the most recent weeks will be an underestimate because of the time lag between onset of symptoms, diagnosis and reporting. For these reasons, figures after week 17 are incomplete. The recent decrease in the number of reported cases is occurring mainly in Luanda and Huambo, the two largest urban areas of the country, following the implementation of vaccination campaigns. However, Benguela, the third most populated urban area in the country, is currently reporting an increasing number of cases, and new areas continue to experience transmission of yellow fever, indicating that the epidemic is not yet under control.

At the time of the investigation, in addition to Luanda province, five provinces have confirmed local transmission (Benguela, Cuanza Sul, Huambo, Huila and Uige). Overall, the three provinces with the highest number of reported cases are Luanda, Huambo and Benguela, corresponding to the provinces where the three largest urban areas are located (see Figure 3):

- As of 23 May 2016, the province of Luanda had reported the highest number of confirmed cases (n=466). The
 outbreak peaked between the last week of February and the second week of March 2016 with more than 50
 confirmed cases reported per week. Since then, the number of cases has decreased, with five cases reported
 for each of the last two weeks of April.
- The province of Huambo, central Angola, reported the second highest number of confirmed cases after Luanda province (n=121). The outbreak peaked between the last week of February and the third week of March, with more than ten confirmed cases reported per week. The number of cases has decreased in recent weeks, with four confirmed cases reported on week 17.
- The province of Benguela is the third most affected after Luanda and Huambo with 66 confirmed cases. The number of confirmed cases reported per week increased during April 2016, with the outbreak peaking in the last week of April with 16 confirmed cases reported.



Figure 3. Distribution of suspected and confirmed cases of yellow fever by province of reporting, Angola, 5 December 2015–22 May 2016

ECDC. Map produced on 24 May 2016

Data source: Ministry of Health, Angola and WHO [25]

Cumulative attack rates during the epidemic period are highest in the two largest urban areas of the country located in the province of Luanda, where the outbreak started in December 2015, and the province of Huambo, affected in February 2016. Urban and peri-urban transmission cycles account for the highest number of cases, but transmission has spread to more rural areas in recent weeks.

Most confirmed cases were in individuals between 15 and 30 years of age and overall 70% were in males. This gender imbalance affects cases above 10 years of age. As is usual in yellow fever outbreaks, under-ascertainment of asymptomatic and mild infections has been documented. In addition, a significant proportion of severe cases may be unreported because private clinics are not consistently integrated into the surveillance system and a significant proportion of the population in Angola regularly resort to traditional medicine.

The identification of suspected yellow fever cases by public health services is further affected by the concurrent malaria epidemic that was particularly intense in the early months of 2016. A study found 47% of 232 confirmed cases of yellow fever positive for malaria. Co-infection of yellow fever with dengue and chikungunya has been identified, even though the laboratory assay used did not enable past and acute infections to be distinguished from one other.

Imported cases from Angola have already been reported to DRC (41 confirmed cases), Kenya (two confirmed cases) and the People's Republic of China (11 confirmed cases).

In response to the epidemic, the first mass vaccination campaigns started on 2 February 2016. As of 15 of May, the International Coordination Group for yellow fever vaccine (ICG) had released 11.7 million doses for Angola. Vaccination campaigns took place throughout the province of Luanda in February and March, and in selected municipalities of Huambo and Benguela provinces in April. Campaigns are currently in progress in selected municipalities of the provinces of Benguela, Cuanza Sul, Huambo, Huíla and Uige. Due to limited vaccine supply, the current yellow fever vaccination strategy focuses on mass vaccination campaigns of the population ≥6 months of age in municipalities where local yellow fever transmission has been confirmed. While areas with local transmission are a priority, the strategy does not allow intervention in as yet unaffected areas in order to prevent establishment of transmission. Vaccine coverage analysis has shown that adult males are less likely to be vaccinated than women and children, potentially explaining the over representation of young males among cases.

Yellow fever vaccine was integrated into routine immunisation in 1980. UNICEF estimated the yellow fever childhood routine vaccination coverage in Angola to be 40–77 % between 2009 and 2014 [26]. Vaccine supplies for routine childhood yellow fever vaccinations are currently insufficient.

Vector control against *Aedes aegypti* is ongoing in urban areas, but is made difficult due to lack of information about the distribution and abundance of the vector in the country.

Situation in the Democratic Republic of Congo (DRC)

As of 23 May, DRC has reported 590 cases of yellow fever, including 48 confirmed cases, of which 41 had a recent travel history to Angola. Two were classified as resulting from sylvatic transmission in Tshuapa and le Bas Uélé provinces in January 2016 and two were autochthonous cases – one in Kinshasa and one in Kongo Central province. Three additional cases are under investigation. Confirmed cases have been reported in the provinces of Kongo central, Kinshasa and Kwango where additional suspected cases are under investigation.

Figure 3. Distribution of yellow fever confirmed cases, by province of reporting, Democratic Republic of Congo, 1 January –23 May 2016



Situation in Uganda

On 20 May 2016, WHO issued an update on the yellow fever outbreak in Uganda, which is unrelated to the outbreak in Angola. Between 26 March and 19 May 2016, health authorities reported 60 yellow fever cases, including seven deaths, in the districts of Masaka, Rukungiri, Ntungamo, Bukumansimbi, Kalungu, Lyantonde and Rakai. Seven cases and two deaths were laboratory-confirmed. None of the cases had a recent travel history to Angola [27].

ECDC threat assessment for the EU

The large outbreak of yellow fever in Angola is of concern, given the risk that the virus will be introduced through viraemic travellers to countries at risk of transmission, in particular neighbouring countries with receptive areas. This extension of the epidemic would increase the number of travellers that could be exposed.

The outbreak needs to be controlled in the three countries, Angola, DRC and Uganda in order to prevent further spread in the region and beyond. The number of new suspected and confirmed cases in Angola has been decreasing and a mass vaccination campaign has already reached about half of the targeted population. However, local transmission is still documented in many areas of the country and a potential vaccine shortage is predicted in the coming months. The outbreak in Angola is not yet under control and is currently expanding to additional provinces, posing a further challenge to the ongoing mass vaccination campaign. The possible shortage of the yellow fever vaccine stock pile due to the ongoing outbreak in Angola and the start of vaccination in Uganda and DRC poses a significant potential challenge for the current control strategy.

The rainy season in Angola ends in May, meaning that the conditions favouring vector abundance are likely to decrease in the southern and central provinces, complementing the effect of the ongoing vaccination campaigns and vector control measures in reducing the transmission rate. However, in the northern provinces environmental conditions for mosquito transmission will probably remain suitable, allowing for new cases to occur in the coming months, until the vaccination of the targeted population has reached an 80% coverage level, as recommended by WHO [4].

Currently, all regions in Angola should be considered as areas at high risk of yellow fever transmission. Large urban areas, the province of Cabinda, where acquisition of infection was reported to have occurred for a case identified in the Democratic Republic of Congo (DRC), and provinces in the Angolan northern provinces of Zaire, Uige, Malange and Lunda Norte represent a significant risk for international spread. Imported confirmed cases from Angola have been reported in DRC (41 cases), Kenya (two cases) and the People's Republic of China (11 cases).

In DRC, the confirmation of the autochthonous circulation in the capital is a major concern as Kinshasa is densely populated, posing the risk of extension to Brazzaville, the capital of Republic of the Congo, located across the Congo River.

Risk for travellers and residents to affected areas

Unvaccinated travellers or residents in an epidemic area in Angola, DRC or Uganda are at risk of becoming infected. Of particular concern are individuals who do not fulfil the vaccination criteria, such as new-born babies and people with underlying health conditions, for whom strict individual vector control measures should be enforced to prevent infection. Currently, all regions in Angola should be considered as areas at high risk of yellow fever transmission. Despite an increase in vaccination coverage, areas with low coverage remain at high risk of transmission.

Risk of international spread

The evolution of the situation in Angola, Uganda and DRC is of concern and is, according to WHO, a serious public health event which warrants intensified national action and enhanced international support. The IHR Emergency Committee decided on 19 May 2016 that, based on the information provided, the event does not constitute a Public Health Emergency of International Concern (PHEIC) [20].

The outbreak in Angola is large and the number of yellow fever cases is, given the wide range of severity of its clinical presentation, underestimated. In addition, people in the region frequently travel by road and plane to neighbouring countries. Therefore the risk of exporting the virus to other countries is high. Viraemic patients travelling to areas where suitable vectors and susceptible human populations are present risk causing local transmission. Such areas exist in most of the inter-tropical zones of Africa, the Americas and Asia. Therefore, the risk of international spread within Africa and beyond is currently high.

As yellow fever and dengue fever share the same mosquito vector (*Aedes aegypti*), any area where dengue transmission has been documented could be suitable for local transmission of yellow fever if the virus is introduced by a viraemic traveller. This could be the case in southern China, where dengue virus transmission occurs during the warmer mosquito vector season, leading to local outbreaks in these areas. However, it has to be stated that yellow fever has never been transmitted by the local *Aedes* species in South-East Asia [5].

Risk related to mass gatherings

The Rio de Janeiro 2016 Olympic Games (5–21 August 2016) and the Paralympic Games (7–18 September 2016) are the two most prominent mass gathering events that will take place in the Americas in the coming months. ECDC has published a specific risk assessment on these events, including an assessment for yellow fever virus infection [28].

Risk of importation to the EU

As long as the WHO recommendation for travellers from areas experiencing epidemics to be vaccinated against yellow fever is not enforced, the risk of yellow fever being imported into Europe exists, in relation to travellers coming from affected countries who are not vaccinated against yellow fever. They may arrive in the EU/EEA and become viraemic as they develop yellow fever. The risk in relation to returning EU/EEA travellers is limited since they are likely to have been immunised.

The risk of the virus being imported into the local competent vector population in the EU through viraemic travellers from Angola is considered to be moderate but possible, particularly in areas where *Aedes aegypti* is present (Madeira). Potential local transmission of yellow fever in areas where *Aedes albopictus* is present in the EU/EEA cannot be ruled out, following the introduction of the virus through a viraemic traveller. Some EU Overseas Countries and Territories (OCT) and Outermost Regions (OMR) are located in the inter-tropical area with large populations of competent *Aedes aegypti* mosquitoes. In these areas, the likelihood of importation is low because of the limited travel patterns with Angola, but the risk of local transmission would be increased because of vector availability.

There is sufficient capacity in the EU for the detection of yellow fever through several reference laboratories.

Risk of transmission in the EU

The risk of occurrence of yellow fever transmission in the EU/EEA is mainly related to areas where *Aedes aegypti* is present. The mosquito is established in the Overseas Countries and Territories (OCT) and Outermost Regions (OMR) of the EU, located in the yellow fever belt (inter-tropical area), as well as in the Black Sea region of

Europe [29,30]. There are uncertainties about the capacity of *Aedes albopictus* to transmit yellow fever but potential local transmission of yellow fever in areas where *Aedes albopictus* is present in the EU/EEA cannot be ruled out, following the introduction of the virus through a viraemic traveller.

Conclusions and options for response

In the EU/EEA, the risk of yellow fever virus being introduced is limited to unvaccinated viraemic travellers coming from epidemic areas. Given that outbreaks of yellow fever in urban settings have the potential for rapid spread and that significant yellow fever epidemics are ongoing in Angola, DRC and Uganda, EU/EEA Member States should consider a range of options for response.

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 - Sleeping or resting in screened or air-conditioned rooms, or using mosquito nets, at night and during the day.

Options to prevent importation into EU/EEA countries

- Implement the WHO International Health Regulations Emergency Committee recommendation to only allow travellers showing proof of a valid vaccination record for yellow fever to leave Angola. The procedure should also be applied to land and sea borders. Entry screening in the EU, for proof of vaccination, would be of limited value because of the limited availability of direct flights and the high likelihood of indirect travel routes into the EU
- Alternatively, EU Member States, particularly those including areas with established populations of suitable Aedes mosquitoes, could prevent the arrival of viraemic travellers by requesting proof of valid vaccination when issuing a visa.

Options to prevent transmission in EU/EEA countries

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- Clinicians should consider yellow fever among differential diagnoses for travellers returning from affected areas.
- Ensure that clinicians and travel health clinics get updated information about areas with an ongoing yellow fever outbreak to support their diagnosis in travellers returning from those areas.
- Apply strict personal prevention measure against *Aedes* mosquito bites for any suspected and confirmed yellow fever case through the use of a mosquito net in receptive areas for yellow fever transmission (i.e. areas with active competent vectors and human population susceptible to yellow fever infection).
- Implement focal vector control in the areas where unvaccinated viraemic travellers have stayed. This option
 helps to reduce the risk of onward autochthonous transmission in EU/EEA mainland and EU Overseas Countries
 and Territories (OCT) and Outermost Regions (OMR), in areas with presence of yellow fever vectors. The vector
 competence of European Aedes albopictus mosquito populations needs to be assessed.

References

- 1. World Health Organization. List of countries, territories and areas. Yellow fever vaccination requirements and recommendations; malaria situation; and other vaccination requirements. Geneva: WHO; 2015. Available from: http://www.who.int/ith/2015-ith-county-list.pdf?ua=1.
- 2. Gershman M, Staples J. Yellow Fever: US Centers for Disease Control and Prevention. 2015. Available from: <u>http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/yellow-fever</u>.
- Jentes ES. The revised global yellow fever risk map and recommendations for vaccination, 2010: consensus of the Informal WHO Working Group on Geographic Risk for Yellow Fever (vol 11, pg 622, 2011). Lancet Infect Dis. 2012 Feb;12(2):98-.
- 4. World Health Organization. Yellow fever (Fact Sheet) [Internet]. Geneva: World Health Organization; 2016 [cited 26 May 2016]. Available from: <u>http://www.who.int/mediacentre/factsheets/fs100/en/</u>.
- 5. Agampodi SB, Wickramage K. Is there a risk of yellow fever virus transmission in South Asian countries with hyperendemic dengue? Biomed Res Int. 2013;2013:905043.
- 6. Mitchell C. Vector competence of North and South American strains of Aedes albopictus for certain arboviruses: a review. J Am Mosq Control Assoc. 1991;7(3):446-51.
- 7. Miller BR, Ballinger ME. *Aedes albopictus* mosquitoes introduced into Brazil: vector competence for yellow fever and dengue viruses. Trans R Soc Trop Med Hyg. 1988;82(3):476-7.
- 8. Mitchell CJ, Miller BR, Gubler DJ. Vector competence of *Aedes albopictus* from Houston, Texas, for dengue serotypes 1 to 4, yellow fever and Ross River viruses. J Am Mosq Control Assoc. 1987 Sep;3(3):460-5.
- Lourenço de Oliveira R, Vazeille M, Filippis A, Failloux A. Large genetic differentiation and low variation in vector competence for dengue and yellow fever viruses of *Aedes albopictus* from Brazil, the United States, and the Cayman Islands. 2003;69(1):105-14.
- 10. Johnson BW, Chambers TV, Crabtree MB, Filippis AM, Vilarinhos PT, Resende MC, et al. Vector competence of Brazilian *Aedes aegypti* and *Ae. albopictus* for a Brazilian yellow fever virus isolate. Trans R Soc Trop Med Hyg. 2002 Nov-Dec;96(6):611-3.
- 11. World Health Organization. Global Health Observatory data repository: World Health Organization; 2016 [cited 26 May 2016]. Available from: <u>http://apps.who.int/gho/data/node.main.WHS3_50?lang=en</u>.
- Garske T, Van Kerkhove MD, Yactayo S, Ronveaux O, Lewis RF, Staples JE, et al. Yellow Fever in Africa: estimating the burden of disease and impact of mass vaccination from outbreak and serological data. PLoS Med. 2014 May;11(5):e1001638.
- Bae HG, Drosten C, Emmerich P, Colebunders R, Hantson P, Pest S, et al. Analysis of two imported cases of yellow fever infection from Ivory Coast and The Gambia to Germany and Belgium. J Clin Virol. 2005 Aug;33(4):274-80.
- European Centre for Disease Prevention and Control. Annual epidemiological report 2014 Emerging and vector-borne diseases. Stockholm: ECDC; 2014. Available from: <u>http://ecdc.europa.eu/en/publications/Publications/emerging-vector-borne-diseases_annualepidemiological-report-2014.pdf</u>.
- 15. Monath TP. Yellow fever: an update. Lancet Infect Dis. 2001 Aug;1(1):11-20.
- 16. Monath TP. Treatment of yellow fever. Antiviral Res. 2008 Apr;78(1):116-24.
- Domingo C, Escadafal C, Rumer L, Mendez JA, Garcia P, Sall AA, et al. First international external quality assessment study on molecular and serological methods for yellow fever diagnosis. PLoS One. 2012;7(5):e36291.
- Yen C, Hyde TB, Costa AJ, Fernandez K, Tam JS, Hugonnet S, et al. The development of global vaccine stockpiles. Lancet Infect Dis. 2015 Mar;15(3):340-7.
- 19. Lindsey NP, Schroeder BA, Miller ER, Braun MM, Hinckley AF, Marano N, et al. Adverse event reports following yellow fever vaccination. Vaccine. 2008 Nov 11;26(48):6077-82.
- 20. World Health Organization. Meeting of the Emergency Committee under the International Health Regulations (2005) concerning Yellow Fever Geneva2016 [cited 2016 May 19]. Available from: http://www.who.int/mediacentre/news/statements/2016/ec-yellow-fever/en/.

- 21. World Health Organization. Yellow fever Geneva: WHO; 2016 [cited 2016 March 22]. Available from: http://www.who.int/csr/disease/yellowfev/en/.
- 22. United Nations Children's Fund. Yellow Fever Vaccine: Current Supply Outlook [internet]. 2016 [cited 30 May 2016]. Available from: http://www.unicef.org/supply/files/YF_number_3_Supply_Update.pdf.
- 23. Lucey D, Gostin LO. A Yellow Fever Epidemic: A New Global Health Emergency? JAMA. 9 May 2016.
- World Health Organization. Yellow Fever Angola. Disease Outbreak News 12 February. Geneva: WHO; 2016 [cited 22 March 2016]. Available from: <u>http://who.int/csr/don/12-february-2016-yellow-fever-angola/en/</u>.
- World Health Organization Regional Office for Africa. Situation Report: Yellow fever outbreak in Angola, 23 May 2016 Brazzaville: World Health Organization,; 2016 [cited 23 May 2016]. Available from: <u>http://www.afro.who.int/pt/yellow-fever/sitreps/item/8660-situation-report-yellow-fever-outbreak-in-angola-23-may-2016.html</u>.
- 26. United Nations Children's Fund. Yellow Fever Vaccine: Current Outlook. New York: UNICEF; 2015. Available from: <u>http://www.unicef.org/supply/files/Yellow Fever Vaccine Current Outlook March 2015.pdf</u>.
- World Health Organization. Situation report. Yellow fever (24 April 2016) [Internet]. 2016 [cited 24 May 2016]. Available from: <u>http://reliefweb.int/sites/reliefweb.int/files/resources/yf-outbreak-in-angola_sitrep-of-25-april.pdf</u>.
- European Centre for Disease Prevention and Control. Potential risks to public health related to communicable diseases at the Olympics and Paralympics Games in Rio de Janeiro, Brazil 2016 [Internet]. Stockholm ECDC; 2016. Available from: <u>http://ecdc.europa.eu/en/publications/ layouts/forms/Publication_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=1486</u>
- European Centre for Disease Prevention and Control. VectorNet: A European network for sharing data on the geographic distribution of arthropod vectors, transmitting human and animal disease agents [Internet]. Stockholm: ECDC; 2016. Available from: <u>http://ecdc.europa.eu/en/activities/diseaseprogrammes/emerging_and_vector_borne_diseases/Pages/VBOR_NET.aspx</u>
- 30. Medlock JM, Hansford KM, Versteirt V, Cull B, Kampen H, Fontenille D, et al. An entomological review of invasive mosquitoes in Europe. Bull Entomol Res. 2015 Dec;105(6):637-63.