RAPID RISK ASSESSMENT

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

Second update, 13 July 2016

Conclusions and options for response

The risk of yellow fever transmission in the EU/EEA is limited and depends on whether the virus is introduced by unvaccinated viraemic travellers to an area with an established, competent and active mosquito vector population. Given that outbreaks of yellow fever in urban settings have the potential to quickly affect a large number of people and that significant yellow fever epidemics are ongoing in Angola and the Democratic Republic of Congo, EU/EEA Member States should consider a range of options for response.

EU citizens who travel to, or live in, countries where there is evidence of periodic or persistent yellow fever virus transmission, especially those in outbreak-affected regions, should:

- be made aware of the risk of yellow fever;
- check their vaccination status and get vaccinated if needed. Vaccination against yellow fever is recommended from nine months of age for people visiting, or living in, yellow fever risk areas. WHO publishes a list of countries, territories and areas with yellow fever vaccination requirements and recommendations [1], which includes Angola and Democratic Republic of Congo;
- take measures to prevent mosquito bites indoors and outdoors, especially between sunrise and sunset when *Aedes* mosquito vectors are most likely to be 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;
  - sleeping or resting in screened or air-conditioned rooms, or using mosquito nets at night and during the day.

To reduce the risk of adverse events following immunisation, healthcare practitioners should be aware of the contraindications and follow the manufacturers' advice on precautions before administering yellow fever vaccine [2].

Options to prevent importation into EU/EEA countries

- The IHR Emergency Committee has recommended to Member States to consider 'the assurance of yellow fever vaccination of all travellers, and especially migrant workers, to and from Angola and Democratic Republic of Congo'. This action is relevant to all countries with active transmission, and should be applied to air, land and sea borders.
- EU Member States that have areas with established populations of competent *Aedes* mosquitoes should consider reducing the risk of viraemic travellers arriving from countries with active transmission by requiring proof of yellow fever vaccination from individuals who apply for visas in the affected countries.

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Options to prevent transmission in EU/EEA countries

- Raise awareness among public health stakeholders, in particular physicians and health professionals working in travel health clinics, about the risk of yellow fever virus introduction to the EU through unvaccinated viraemic travellers from epidemic areas.
- Clinicians should consider yellow fever in the differential diagnoses of travellers returning from areas at risk of yellow fever.
- Ensure that physicians, health professionals 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.
- In receptive areas (i.e. areas with active competent vectors and people susceptible to yellow fever infection), use personal protective measures, such as mosquito nets, for any suspected, probable or confirmed yellow fever case in order to prevent further transmission through mosquito bites.
- Implement focal vector control in all areas where unvaccinated viraemic travellers have stayed in order to prevent further transmission in receptive areas.

Source and date of request

ECDC internal decision, 28 June 2016

Public health issue

This document assesses the risk to EU/EEA countries and citizens associated with the ongoing outbreaks of yellow fever in Angola, Democratic Republic of Congo (DRC) and Uganda, and also includes a brief overview of yellow fever transmission in other parts of Africa.

This is the second update of the rapid risk assessment of the yellow fever outbreaks in Angola, Democratic Republic of Congo and Uganda. The initial risk assessment was published on 25 March 2016 [3]; the first update was published on 30 May [4].

Consulted experts

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Experts from the following institutions contributed to this risk assessment: World Health Organization Headquarters, Directorate-General for European Civil Protection and Humanitarian Aid Operations (European Commission).

ECDC acknowledges the valuable contributions of all experts. Experts from the World Health Organization (WHO) reviewed the risk assessment but their views, as 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.

Disease background information

Yellow fever is an acute viral haemorrhagic disease that affects humans and non-human primates. The virus is transmitted between humans mainly by the *Aedes aegypti* mosquito vector. For more information about transmission, pathology, epidemiology and significant outbreaks of yellow fever in the past, please consult previous ECDC risk assessments [3,4], Annex 1 of this risk assessment, the ECDC factsheet for health professionals, and the WHO yellow fever factsheet .

Event background information

Angola

Outbreak situation

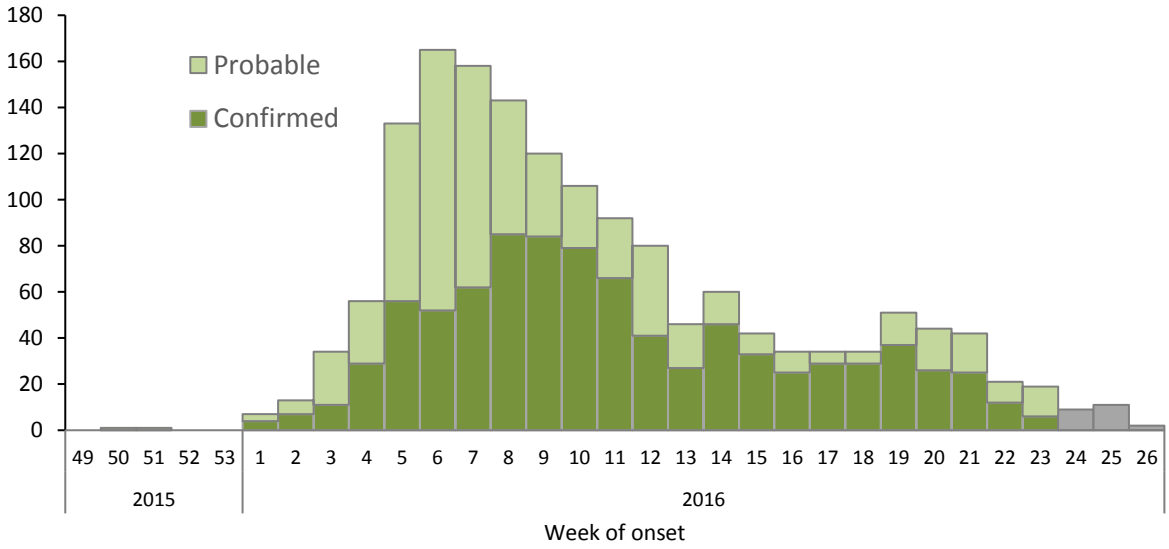
On 21 January 2016, the IHR focal point in Angola notified WHO about an ongoing yellow fever outbreak. The first cases reported were two males living in the municipality of Viana, a densely populated municipality on the outskirts of Luanda. The first case presented with yellow fever symptoms to a private clinic on 5 December 2015 [5,6].

From 21 January to 1 July 2016, the Angolan Ministry of Health notified 3 552 yellow fever cases, 875 of which were laboratory confirmed and 355 were fatal. The case–fatality ratio among confirmed cases is 13.4% (117 of 875) and 10% overall. All provinces in Angola have reported cases during the outbreak.

Since the last rapid risk assessment on yellow fever dated 27 May 2016, which was based on data available up to 22 May, there has been an increase of 1 016 yellow fever cases, including 128 confirmed cases.

The epidemic curve (Figure 1) shows that the highest number of suspected and confirmed cases was reported in February and March 2016, with a peak of notifications of more than 80 confirmed cases reported per week at the end of February. Since April, the number of new cases has declined.

Figure 1. Distribution of probable and confirmed yellow fever cases per week of onset of symptoms, Angola, 5 December 2015–1 July 2016



Note: Data from greyed columns are incomplete due to reporting delays. Data source: [7]

The epidemic curve should be interpreted with caution because of under-ascertainment and underreporting, particularly during the early stages of the epidemic. Many yellow fever infections are asymptomatic or result in mild disease. A significant proportion of severe cases may not be reported in Angola because private health clinics are not consistently integrated into the surveillance system and a significant proportion of the population regularly resort to traditional medicine [8].

The three provinces with the highest number of reported cases are Luanda (1 927 cases including 211 deaths), Huambo (578 cases including 44 deaths) and Benguela (345 cases including 30 deaths), corresponding to the provinces where the three largest urban areas are located.

The recent decrease in the number of reported cases is mainly due to a drop in incidence in Luanda, Huambo and Benguela following the vaccination campaigns in these areas. Six provinces have reported cases with date of onset after 1 June: Benguela, Cuanza Norte, Huila, Luanda Norte, Malange, and Zaire. The most recent confirmed case was reported from Zaire province. In the past three weeks (24 to 26), no new districts reported locally acquired cases. Urban and peri-urban transmission cycles account for the highest number of cases, but transmission has spread from urban to rural areas after the epidemic peaked. Imported cases from Angola have been reported by the DRC (59 confirmed cases), Kenya (two confirmed cases) and China (11 confirmed cases).

Vaccination campaign

Yellow fever vaccine was integrated into routine immunisation in Angola in 1980. UNICEF estimated the yellow fever childhood routine vaccination coverage in Angola to be 40–77% between 2009 and 2014 [9]. Vaccine supplies for routine childhood yellow fever vaccinations are currently insufficient.

The first mass vaccination campaigns in response to the current epidemic started on 2 February 2016. As of 15 May, the International Coordination Group for yellow fever vaccine 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.

As of 1 July, 11 500 000 people have been vaccinated in Angola, out of a target of 15 000 000 people to be vaccinated (population 24 277 000) [7,10]. In the past weeks, additional districts in the affected provinces of Malange, Uige and Zaire have started vaccination. However, the final round of vaccination in Luanda has been delayed.

WHO vaccination focuses on two main strategies: reactive vaccination campaigns in areas with confirmed yellow fever transmission (complemented with catch-up campaigns in areas that report autochthonous transmission after vaccinations campaigns) and pre-emptive vaccination campaigns in high-risk and border areas.

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

Democratic Republic of Congo

Outbreak situation

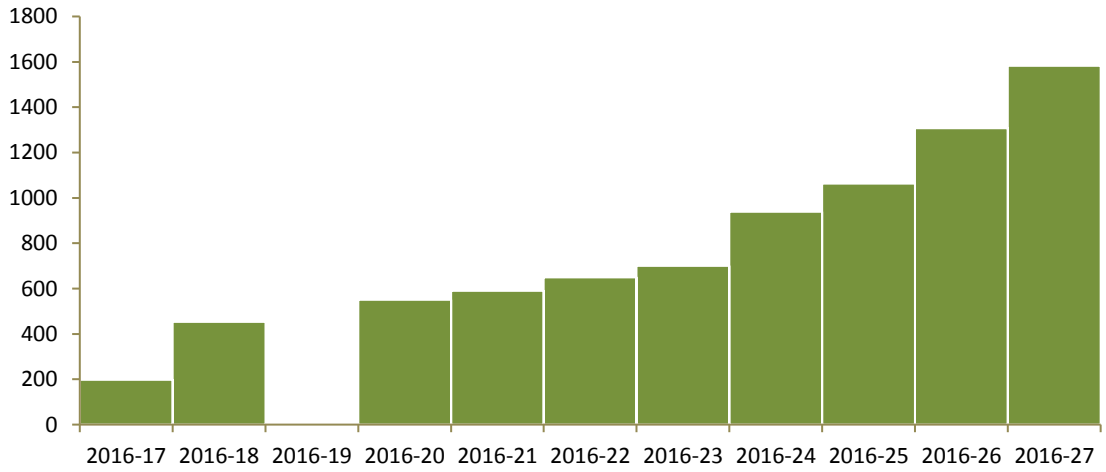
Between 1 January and 1 July 2016, the Democratic Republic of Congo (DRC) reported 1 582 suspected cases of yellow fever, including 68 confirmed cases, 59 of which had a recent travel history to Angola. Of the 1 582 cases, 75 have died since the beginning of the outbreak. The cumulative number of suspected cases is reported in Figure 2. In the past two weeks (26 and 27), the DRC ministry of health reported an increase of around 250 suspected yellow fever cases per week.

Among the cases without recent travel history to Angola, six cases in Kinshasa province, one case in Kongo-Central and two cases in Kwango are reported as autochthonous. In addition, since the beginning of the year, two independent sylvatic cases have been notified, one in Bas-Uele province and one in Tshuapa province. These two cases are not related to the current outbreak in Angola and in other provinces in DRC [11,12].

Vaccination campaign

As of 30 June, 5 500 000 people have been vaccinated in the DRC in Kinshasa, Kongo-Central and Kuango provinces [13].

Figure 2. Cumulative number of reported yellow fever cases in DRC, week 17 to 27, 2016



Note: No data available for week 19

Other countries in Africa with recent or ongoing yellow fever transmission

Situation reports giving the number of cases and deaths in countries affected by yellow fever are available from the WHO emergencies webpages (Yellow fever situation report) [14].

Central Africa

Republic of Congo: According to the WHO weekly report, two suspected cases of yellow fever were reported in the Republic of Congo (as of 30 June) [13]. Bouenza department, which reported the cases, has a border with the Democratic Republic of Congo. The laboratory results are pending.

East Africa

Uganda: There is an ongoing outbreak of yellow fever in Uganda that is not linked to the outbreaks in Angola and the DRC. Between 26 March and 8 June 2016, health authorities reported 91 cases, including seven deaths, in the districts of Masaka, Rukungiri, Ntungamo, Bukumansimbi, Kalungu, Lyantonde and Rakai. Seven cases including two deaths were laboratory confirmed. None of the cases had a recent travel history to Angola [15].

West Africa

Chad: The most recent reported case had onset of symptoms in January 2016 [13] and was classified as sylvatic transmission.

Cameroon: Cameroon has reported 944 suspected cases of yellow fever since the beginning of 2016 [16]. The cases are reported in eight of the country's ten regions; 55 were IgM positive for yellow fever, including 14 unvaccinated people and 12 of unknown vaccination status. Cameroon reported 789 cases in 2015. Yellow fever vaccination coverage was 80% in 2014 according to the annual GAVI report [17].

Ghana: Sporadic sylvatic cases were reported in 2015 and 2016 according to the WHO weekly report published on 30 June 2016.

Guinea: As of 30 June, 39 suspected cases had been reported in Guinea in 2016 according to WHO. Investigations are ongoing.

Risk management activities and priorities in affected countries

Yellow fever outbreaks should be rapidly controlled in order to prevent spread in the country, the region and beyond. This is particularly important for outbreaks in urban areas, such as in Angola and the DRC. The Incident Management System under WHO's new emergency programme has been activated for the yellow fever outbreaks in Angola and the DRC. The WHO Strategic Response Plan (June–August 2016) guides the international response to the current yellow fever outbreaks in Angola, the DRC and Uganda, as well as countries preparing for the possible importation of yellow fever cases [18].

Resurgence of yellow fever disease in densely populated urban areas, as illustrated by the current outbreak of yellow fever in the DRC and Angola, and the large geographical spread of cases have increased the demand for vaccines for emergency response vaccination, which challenges the already dire supply situation [19]. In order to mitigate potential shortages in yellow fever vaccine due to the outbreak in Angola and the DRC, WHO published a statement on the use of lower doses of yellow fever vaccine in emergencies [20]. The proposed fractional dosing do not apply to routine immunisation campaigns and is seen as a short-term measure in the context of a potential vaccine shortage for use in emergencies. The Strategic Advisory Group of Experts on Immunization found that

> 'the available evidence is sufficient to determine that fractional dosing of yellow fever vaccine to one fifth of the standard dose (0.1 ml instead of 0.5 ml) could be a safe and effective option for mass vaccination campaigns to control urban outbreaks in situations of acute vaccine shortage'.

ECDC threat assessment for the EU

The report from the joint ECDC–European Commission mission to Angola Assessing the yellow fever outbreak in Angola (10–20 May 2016) summarises the epidemiological situation of yellow fever in Angola up to the end of May 2016, reports on the implemented control measures, evaluates the risk of importation of yellow fever to the EU, assesses the risk for EU citizens, and provides advice to the Angolan government and the European Commission [8].

The outbreaks in Angola and the DRC continue to be of concern, given the risk that the virus will be exported through viraemic travellers and introduced to countries at risk of vector-borne transmission. The risk is highest for countries that share borders with the DRC and Angola but exists also for distant countries with competent vector populations (receptive areas). An extension of the epidemic would increase the number of travellers potentially exposed.

In Angola, the number of new suspected and confirmed cases has been decreasing and the mass vaccination campaigns are estimated to have reached about 75% of the targeted population. The current information indicate that the outbreak in Angola is progressively being brought under control. Vaccination activities are continuing in urban centres and high-risk areas. Transmission in urban centres in the northern Angolan provinces of Zaire, Uige, Malange and Lunda Norte continues to represent a significant risk for international spread pending the full achievement of the emergency vaccination campaigns. Transmission may still spread to, or flare up in, areas not yet fully covered by vaccination campaigns.

Laboratory confirmation of autochthonous transmission in Kinshasa means that the outbreak has spread to the capital of the Democratic Republic of Congo. This is of major concern, not only for the population in Kinshasa but also for the Brazzaville, the capital of the Republic of the Congo, which is located across the Congo River. Both cities are densely populated and at risk of rapidly evolving outbreaks.

The outbreak in the DRC is evolving, and the number of weekly suspected cases have increased in the past three weeks. Underreporting of the mild form of yellow fever is expected. Recent figures on the number of confirmed yellow fever cases are likely to be underestimated because of delays in laboratory confirmation and a lack of reagents for the central laboratory [12]. A vaccination campaign has started and will be extended over the coming weeks, especially in Kinshasa.

The control of the yellow fever outbreaks in Angola and DRC will depend on the availability of vaccine and how and effectively vaccination is implemented.

Risk for travellers and residents to affected areas

Unvaccinated travellers or residents in an epidemic yellow fever area are at risk of becoming infected. Of particular concern are individuals who cannot be vaccinated because they do not meet the vaccination criteria, e.g. newborns and people with underlying health conditions, for whom strict individual vector control measures should be enforced to prevent infection.

Risk of international spread

The evolution of the situation in Angola and the DRC is of concern. The IHR Emergency Committee decided on 19 May 2016 that the urban yellow fever outbreaks in Angola and the DRC are a serious public health event which deserve intensified national action and enhanced international support. The Committee also decided that, based on the currently available information, the event does not constitute a Public Health Emergency of International Concern [21].

On 19 May 2016, the IHR Emergency Committee also recommended to Member States to consider 'the assurance of yellow fever vaccination of all travellers, and especially migrant workers, to and from Angola and Democratic Republic of Congo'.

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.

The outbreaks in Angola, the DRC and Uganda are significant, affecting large geographic areas including highly populated cities. 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 increase the risk of local transmission. Such areas exist in most of the tropical areas of Africa, the Americas and Asia. Therefore, the risk of international spread within Africa and beyond remains 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. However, it has to be stated that yellow fever has never been transmitted by the local populations of *Aedes aegypti* in south-east Asia [22].

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 and an update on these events, including an assessment for yellow fever virus infection [23,24].

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 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 posed by EU/EEA citizens returning from affected areas is limited because it is likely that they were vaccinated before travelling.

The risk of the virus being imported into the local competent vector population in the EU through viraemic travellers from Angola or the DRC is considered to be moderate but possible in areas where *Aedes aegypti*, the primary vector of yellow fever in urban settings, is present (Madeira, Portugal). Some EU Overseas Countries and

Territories and Outermost Regions are located in the tropics 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, the DRC or Uganda, 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 a number of 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 and Outermost Regions of the EU, located in the so-called yellow fever belt in the tropics, as well as in the Black Sea region [25,26].

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.

Risk of transmission via substance of human origin*

Transmission of yellow fever through blood or plasma transfusion and transplantation has not been reported. The yellow fever 17D vaccine has been transmitted through transfusion of blood donated by recently immunised donors [27]. As only 15–25% of people infected with yellow fever develop symptoms, asymptomatic donors may donate infectious blood. Moreover, yellow fever virus survives in blood preserved with citrate for 35 days and for 60 days if preserved with glycerol [28]. Thus, the risk of yellow fever transmission through donated blood cannot be excluded. Data related to the risk of yellow fever transmission through tissues and cells, and organs are not available.

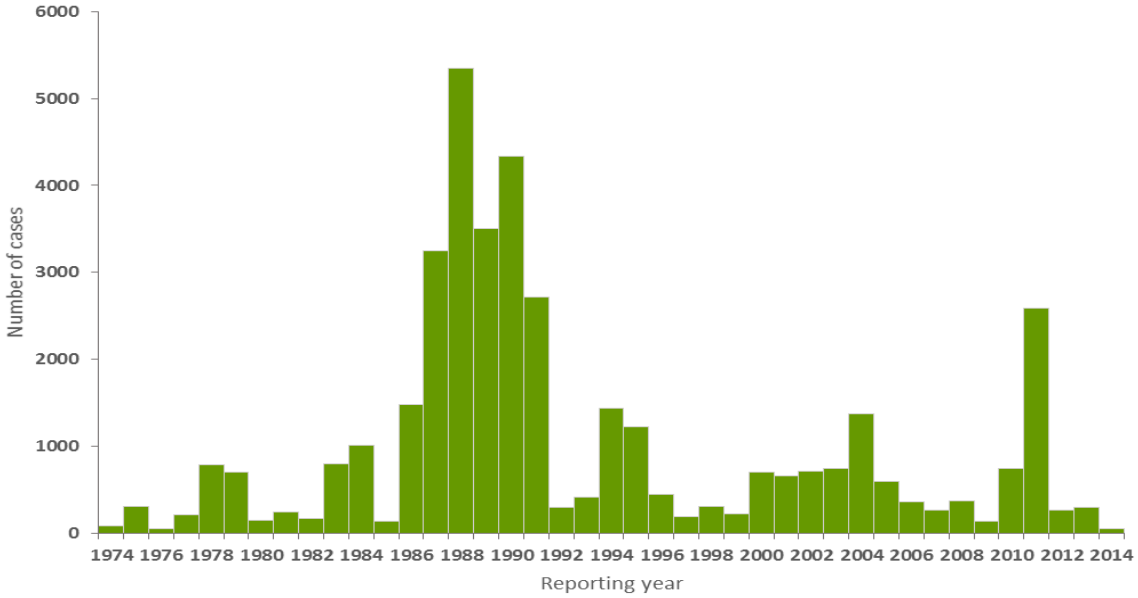
Prospective SoHO donors with a history of yellow fever may donate blood 14 days after full recovery. Donation of SoHO is permitted four weeks after vaccination with attenuated viral vaccine [29]. It should be noted that current yellow fever outbreaks are occurring in malaria-endemic areas. The deferral period for blood donors returning from areas affected by malaria will be sufficient to prevent the donation of yellow-fever-infected blood.

Yellow fever vaccination is contraindicated for immunocompromised patients after solid organ and haematopoietic stem cell transplantation. Patients living in countries endemic for yellow fever, or patients planning to travel in endemic countries, should be immunised before transplantation.

* Substances of human origin (SoHO) are human blood, blood components, tissue, cells or organs as defined in Directive 2002/98/EC, Directive 2004/23/EC and Directive 2010/53/EU.

Annex 1: Annual number of yellow fever cases reported to WHO (1974–2014)

Figure 1. Worldwide distribution of yellow fever cases reported to WHO, 1974–2014



Data source: WHO Global Health Observatory data repository

Between 1987 and 1991, recurrent yellow fever outbreaks with more than 17 000 cases were notified in Nigeria. 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), the other in 1988 (37 cases) [30].

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