



RAPID RISK ASSESSMENT

Outbreak of Ebola virus disease in West Africa

Seventh update, 17 October 2014

Main conclusions and options for risk reduction

Since December 2013, and as of 12 October 2014, 8 997 cases of EVD, including 4 493 deaths, have been reported by the World Health Organization (WHO) in seven reporting countries (Guinea, Liberia, Nigeria, Senegal, Sierra Leone, Spain and the USA). One additional case was reported by the USA on 14 October in a second healthcare worker in Dallas, Texas, who tested positive for Ebola virus after having cared for the first case in the USA.

On 6 October, the Spanish authorities reported a confirmed case of Ebola virus disease (EVD) in a healthcare worker who cared for a patient with Ebola infection repatriated to Spain. The ongoing investigation in Spain is providing information to further understand how the infection was transmitted to this healthcare worker. There is currently no evidence indicating that the healthcare-associated transmission resulted from a change in the transmissibility of the virus. The current recommended infection control measures remain appropriate, if strictly applied. While additional cases among the contacts of the infected nurse cannot be excluded at this time, it is considered extremely unlikely that the event will result in significant spread in Spain.

The evolving epidemic of EVD over the last weeks increases the likelihood that EU residents and travellers to the EVD-affected countries will be exposed to infected or ill persons. The risk of infection for residents and visitors in the affected countries through exposure in the community is considered low if they adhere to the recommended precautions. Residents and visitors to the affected areas run a risk of exposure to EVD in healthcare facilities. The level of this risk is related to how well the infection control measures are being implemented in these settings and the nature of the care required.

As the epidemic is still evolving and more staff is deployed in the affected countries to support the epidemic control, the risk of importation of EVD cases to the EU is increasing. The risk of Ebola virus spreading from an EVD patient who arrives in the EU as result of a planned medical evacuation is considered to be low when appropriate measures are strictly adhered to, but cannot be excluded in exceptional circumstances. The transmission to a healthcare worker in Spain illustrates the connection between the epidemic in West Africa and the risk for the EU, and further stresses the need to control the epidemic in West Africa.

If a symptomatic case of EVD presents in a EU Member State, secondary transmission to caregivers in the family and in healthcare facilities cannot be excluded. This may happen in particular at an early stage of the disease, when patients are not yet very contagious but unprotected contacts are occurring, and at a late stage of the disease, after EVD is confirmed, when patients may experience very high viral loads while undergoing contamination-prone invasive procedure in intensive care units.

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The options for risk reduction are:

- To reduce the risk of infection in West Africa the following options are available: avoid non-essential travel to the affected areas and strictly follow the EVD prevention measures in communities. As there is an increased risk of infection in healthcare facilities, visitors to the EVD-affected countries should identify appropriate incountry healthcare resources prior to travelling.
- To reduce the risk of importation to the EU, the WHO recommendations related to the declaration of a Public Health Event of International Concern (PHEIC) should be applied, in particular effective exit screening. Screening cannot detect infected cases still incubating and not yet presenting with symptoms.
- Based on the evidence of the validity of methods currently available for entry screening at major points of entry, and the likely prevalence of screening-detectable cases among those who have undergone exit screening, the added value of entry screening, if exit screening is being conducted effectively, is likely to be very small, and the resource implications considerable. In the absence of an evaluation of the performance of exit screening, entry screening remains an option to be considered.
- To reduce the risk of transmission within the EU following importation of Ebola virus, the following options are available: epidemic control based on interruption of transmission by infection control measures and implementation of isolation and treatment of patients, and monitoring and contact tracing of contacts; raising awareness and sensitising healthcare providers in the EU about EVD, and supporting them with resources that will help them identify and manage potential EVD patients; enhancing information and communication to travellers departing from EVD-affected countries.
- Transmission to healthcare workers can be prevented by the strict application of infection control measures as recommended by WHO. However, even when infection control measures are thoroughly applied, transmission to healthcare workers can still exceptionally occur. Infection of a healthcare worker may result from a breach in the strict application of the infection control measures, when caring for an infectious patient, when involved in waste management or when removing personal protective equipment (PPE).

Tools that need to be considered for the optimisation of the safe management of patients include regularly repeated hands-on training in the use of PPE, the performance of simulation exercises, continuous supervision and monitoring of both the care of the patient and the putting on and removal of PPE and working in pairs (buddy system). Transfer of the patient to a specialised high level isolation unit is an option that may be considered, taking into account availability, feasibility and the safety of transfer.

Source and date of request

Internal decision, 16 October 2014.

Public health issue

To update the assessment of the risk of importation and transmission of Ebola virus in the EU associated with the epidemic of Ebola virus disease in West Africa currently affecting Guinea, Liberia, Sierra Leone, Spain and the United States of America. We add evidence on the risks of transmission and on hospital infection control, since three healthcare workers having cared for EVD patients outside of West Africa have become infected.

This assessment does not cover the ongoing EVD epidemic in the Democratic Republic of Congo or the outbreak of Marburg virus disease in Uganda.

The current EVD outbreak was first assessed in an ECDC rapid risk assessment entitled 'Outbreak of Ebola haemorrhagic fever in Guinea', dated 23 March 2014 [1]. Detailed information about the Ebola virus and the epidemiology of EVD can be found in a series of ECDC publications that are available on the ECDC website [1-7].

Consulted experts

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Disease background information

Infections with Ebola viruses originating from Africa cause a severe disease in humans called Ebola virus disease. There are five species of the genus Ebolavirus (Filoviridae family): Zaïre ebolavirus, Sudan ebolavirus, Reston ebolavirus, Taï Forest ebolavirus and Bundibuqyo ebolavirus [8,9]. The current outbreak in West Africa is caused by Zaire ebolavirus. A concurrent EVD outbreak was declared on 26 August 2014 in the Democratic Republic of Congo. The two outbreaks are not connected [10].

Ebola viruses are biosafety level-4 pathogens (BSL-4; risk group 4) and require special containment measures and barrier protection, particularly for healthcare workers. The viruses can survive in liquid or dried material for many days [11]. They are inactivated by gamma irradiation, heating for 60 minutes at 60 °C or boiling for five minutes, and are sensitive to sodium hypochlorite (bleach) and other disinfectants [12,13]. Freezing or refrigeration will not inactivate Ebola viruses [14,15].

The incubation period (the period between infection and first symptoms) is usually four to ten days but can be as short as two days and as long as 21 days. The case-fatality ratio for Zaire ebolavirus infections is estimated to be between 44% and 90% [16].

Ebola viruses are highly transmissible by direct contact with infected blood, secretions, tissues, organs and other bodily fluids from dead or living infected persons [17]. Transmission via inanimate objects contaminated with infected bodily fluids (fomites) is possible [18]. The principal mode of transmission in human outbreaks is personto-person transmission through direct contact with a symptomatic or dead EVD case (Table 1). Airborne transmission has not been documented [19].

The probability of transmission is considered low in the early phase of human disease (i.e. the prodromal phase) [16]. Risk of transmission may increase with transition to later stages of the disease. During an Ebola outbreak in DRC, the most important risk factor was direct physical contact with an infected sick person. The risk was higher with exposure to bodily fluids during the late stages of the disease [20]. EBOV is shed in a wide variety of bodily fluids during the acute period of illness [21,22]. A marked difference in viral load, especially early in the course of disease, was previously observed with Zaire ebolavirus between survivors and non-survivors with high levels of viraemia associated with poor outcomes [21].

Burial ceremonies and handling of dead bodies play an important role in transmission [23]. Ebola virus genome has been detected in semen up to 91 days after onset of disease [24], and replicative Ebola virus has been detected in semen 41 days after onset of disease [17,25].

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Type of contact	Type of contact				
Low risk	• Casual contact with a feverish but ambulant and self-caring patient, e.g. sharing a seating area or public transportation; receptionist tasks.				
High risk	• Close face-to-face contact (e.g. within one metre) without appropriate personal protective equipment (including eye protection) with a probable or confirmed case who is coughing, vomiting, bleeding, or who has diarrhoea; or has had unprotected sexual contact with a case up to three months after recovery.				
	• Direct contact with any material soiled by bodily fluids from a probable or confirmed case;				
	• Percutaneous injury (e.g. with needle) or mucosal exposure to bodily fluids, tissues or laboratory specimens of a probable or confirmed case.				
	• Participation in funeral rites with direct exposure to human remains in or from an affected area without appropriate personal protective equipment.				
	• Direct contact with bushmeat or bats, rodents, primates, living or dead in/from affected areas.				

Table 1. Levels of risk of transmission of Ebola viruses according to type of contact with an infected patient

Treatment and vaccine development

No specific treatments or vaccines are presently available for EVD. However, early supportive treatment can improve the chances of recovery [26]. Potential new Ebola therapies and vaccines were reviewed during two WHO meetings on 4–5 and 29-30 September 2014 and further assessed by scientific review [27,28]. Several of these potential drugs have in the past month been used in experimental treatment of individual EVD cases.

During the first WHO consultation meeting, there was consensus that the use of whole blood therapies and convalescent blood serums needs to be considered as a matter of priority [29].

A number of candidate treatments have shown promise in non-human primate models, although none of these drugs are licensed for treatment of EVD and their availability is currently limited.

In addition, the first WHO consultation meeting identified two vaccines in advanced stages of development:

- a recombinant vesicular stomatitis virus vaccine expressing a Zaire surface glycoprotein (rVSV-ZEBOV), which
 induces a Zaire ebolavirus specific immune response; and
- a non-replicative chimpanzee adenovirus type 3 vaccine (cAd3-ZEBOV) also containing the gene for the Zaïre ebolavirus surface glycoprotein.

Phase 1 and 2 trials have been initiated in the USA, in Africa and Europe with the goal of assessing immunogenicity and safety. It is unlikely that efficacy data will be available before a fast-track authorisation of the vaccines. If proven safe, a vaccine could be available in the coming months for priority use in healthcare workers. However, it should be noted that if the vaccines are rolled out, they will have undergone limited testing in humans, and postauthorisation monitoring of safety and efficacy will be important.

The European Medicines Agency (EMA) has started to review available information on a larger panel of Ebola treatments currently under development in order to support fast-track authorisation in the EU/EEA and decision-making by health authorities [30].

Event background information

Chronology of events – key dates

22 March 2014: the Guinea Ministry of Health notified WHO about a rapidly evolving outbreak of EVD [31]. The first cases occurred in December 2013. The outbreak is caused by a clade of *Zaïre ebolavirus* that is related but distinct from the viruses that have been isolated from previous outbreaks in central Africa, and clearly distinct from the *Taï Forest ebolavirus* that was isolated in Côte d'Ivoire from 1994–1995 [23,32,33]. The first cases were reported from south-eastern Guinea and the capital Conakry.

May 2014: the first cases were reported from Sierra Leone and Liberia [34,35] to where the disease is assumed to have spread through the movement of infected people over land borders.

End of July 2014: a symptomatic case travelled by air to Lagos, Nigeria, where he infected several healthcare workers and airport contacts before his condition was recognised to be EVD.

8 August 2014: WHO declared the outbreak a Public Health Event of International Concern (PHEIC) [36] and confirmed on 22 September that the 2014 Ebola outbreak in West Africa continued to constitute a PHEIC.

29 August **2014**: the Ministry of Health in Senegal reported a confirmed imported case of EVD in a 21-year-old male native of Guinea.

18 September 2014: the United Nations Security Council recognised the EVD outbreak as a 'threat to international peace and security' and unanimously adopted a resolution on the establishment of an UN-wide initiative which focuses assets of all relevant UN agencies to tackle the crisis [37].

23 September 2014: A study published by the WHO Ebola response team forecasted more than 20 000 cases (5 740 in Guinea, 9 890 in Liberia, and 5 000 in Sierra Leone) by the beginning of November 2014 [38]. The same study estimated the doubling time of the epidemic at 15.7 days in Guinea, 23.6 days in Liberia, and 30.2 days in Sierra Leone.

30 September 2014: the US Centers for Disease Control and Prevention (CDC) announced the first imported case in the USA of EVD linked to the current outbreak in West Africa.

3 October 2014: in Senegal, all contacts of the imported EVD case had completed the 21-day follow-up period without developing disease. No local transmission of EVD has been reported in Senegal. The imported case tested negative on 5 September, and WHO declared Senegal free of Ebola on 17 October 2014 (two incubation periods after the last isolated case tested negative).

6 October 2014: The Spanish authorities reported a confirmed case of Ebola virus disease (EVD) in a healthcare worker who cared for the second Spanish patient repatriated to Spain with EVD.

10 October: A healthcare worker at Texas Health Presbyterian Hospital who provided care for the Ebola patient hospitalised (see above milestone: 30 September 2014) tested positive for Ebola [39].

14 October: A second healthcare worker at Texas Health Presbyterian Hospital who provided care for the first Ebola patient tested positive for Ebola and was hospitalised.

Epidemiological update

Situation in West Africa

Since December 2013 and as of 12 October 2014, 8 994 cases of EVD, including 4 492 deaths, have been reported by WHO (Figure 1) [40].

The distribution of EVD cases by affected countries is as follows and is presented in Figure 1:

- Guinea: 1 472 cases and 843 deaths as of 12 October 2014;
- Liberia: 4 249 cases and 2 458 deaths as of 11 October 2014;
- Sierra Leone: 3 252 cases and 1 183 deaths as of 12 October 2014;
- Nigeria: 20 cases and 8 deaths, with last confirmed case in Lagos on 5 September 2014 (37 days as of 12 October 2014) and in Rivers State on first September 2014 (41 days as of 12 October);
- Senegal: 1 case, no deaths, confirmed on 28 August 2014 (45 days as of 12 October). All contacts have completed 21 days of follow-up.

Figure 1. Distribution of cases of EVD by week of reporting in Guinea, Sierra Leone, Liberia, Nigeria and Senegal, weeks 48/2013 to 42/2014*, n= 8 994



* The bar for week 42/2014 does not represent a complete week. The solid green line represents the trends based on a five week moving average plotted on the fifth week of the moving average window. The figure includes one imported case in Senegal [40].

The WHO Ebola response team showed that the current EVD cases present a similar course of infection, signs and symptoms when compared with previous outbreaks of EVD [38]. The incubation period was estimated to be 11.4 days with serial interval of 15.3 days. The case–fatality ratio estimated among 4 010 cases with known clinical outcome in Guinea, Liberia and Sierra Leone was 70.8% (95% CI: 68.6–72.8%) with no noticeable difference between the countries.

Situation in Guinea, Sierra Leone and Liberia

Guinea, Liberia and Sierra Leone are experiencing widespread intense transmission as per WHO categorisation [40]. The outbreak is still evolving in these three countries (Figures 2 and 3). Officially reported figures are believed to be underestimates, especially in Liberia and particularly in Monrovia [38,40]. The incidence is increasing in Guinea, notably in Coyah prefecture neighbouring Conakry. Macenta is still experiencing significant transmission, new cases are reported in Beyla and Lola prefecture neighbouring Ivory Coast, and in Boke neighbouring Guinea Bissau in the west. The most active transmission areas in Sierra Leone are Freetown and Western areas (urban and rural), the surrounding Bombali and Porto Loko districts, and Bo and Tonkolili districts.





* The bar for week 42/2014 does not represent a complete calendar week.

Source: Data are based on official information reported by ministries of health up to the end of 12 October for Guinea and Sierra Leone and 11 October for Liberia [40].



Figure 3. Distribution of cases of EVD by week of reporting in Guinea, Sierra Leone, Liberia and Nigeria (as of week 41/2014)

Source: Data from ministries of health reports (probable and confirmed cases).

Situation in Nigeria

As of 12 October 2014, 20 cases, including eight deaths have been notified[40]. The last case in Lagos was confirmed on 5 September 2014 and in Rivers State on 1 September 2014 [41]. All 891 identified contacts in Nigeria have completed the 21-day follow-up (362 contacts in Lagos, 529 contacts in Port Harcourt) [42].

Situation among healthcare workers in West Africa

As of 12 October 2014, WHO reported 425 healthcare workers infected with EVD of whom 236 died [40]. Table 2 details the distribution of cases and deaths among healthcare workers in the four affected countries.

Country	Healthcare worker cases (% of reported cases)	Healthcare worker deaths (% of reported deaths)		
Guinea	76 (5.2)	40 (4.7)		
Liberia	209 (4.9)	96 (3.9)		
Sierra Leone	129 (4.0)	95 (8.0)		
Nigeria	11 (55.0)	5 (62.5)		
Total	425 (4.7)	236 (6.0)		

Source: data are based on official information reported by ministries of health as of 12 October for Guinea and Sierra Leone and 11October for Liberia [40].

Médecins Sans Frontières reported that from March to 26 September, 14 of their healthcare workers, including one international staff member, had been infected; eight of whom died [43].

Situation outside West Africa

USA

On 30 September 2014, the US CDC announced the first imported case of EVD linked to the current outbreak in West Africa. The individual who had recently arrived from Liberia was diagnosed in Dallas, Texas. This person was not a healthcare worker and was visiting relatives in the USA. He is reported to have had a high-risk exposure in Liberia prior to travelling. He was reported to be asymptomatic when leaving West Africa and remained asymptomatic while travelling and upon arrival in the USA on 20 September. He developed symptoms around 24 September, sought medical care on 26 September, and was hospitalised and isolated on 28 September 2014. He died on 8 October 2014.

The US health authorities are investigating contact persons who may have been at risk of infection from this patient. This excludes people that were on the same commercial airlines because the person was asymptomatic while travelling from Liberia to the USA. The person reported developing symptoms only several days after the flights and therefore was not contagious during that period.

As of 7 October 2014, the US CDC reports that the investigation of 10 contact persons with definite exposure to the case and 38 persons with possible exposure is ongoing. It was reported that daily monitoring of contacts would be carried out for up to 21 days after exposure to the case to check for fever and other symptoms [44].

The second confirmed case identified in Dallas on 10 October is a healthcare worker who participated in the management of the imported case who travelled from Liberia and was diagnosed in Dallas, Texas [39].

The third case in the USA, confirmed on 14 October, was a second health care worker at Texas Health Presbyterian Hospital who provided care for the first Ebola patient diagnosed in the USA [45]. The Centers for Disease Control and Prevention confirmed that the case travelled by air on 13 October, the day before reporting symptoms. Because of the proximity in time between the evening flight and first report of illness the following morning, CDC is contacting the 132 passengers on the Frontier Airlines flight. According to media, the patient has been transferred to Emory University Hospital in Atlanta [46].

Clinicians in the United States have reported that patients in the advanced phase of the disease have an increased bodily fluid output of about five to ten litres per day, in combination with viral shedding in most bodily fluids (and skin). Virus was not, however, found in the dialysate of one patient where this was examined. No virus was detected on sampled surfaces of the toilet, bathroom or highly touched areas in the patient room. [47]

Spain

On 6 October, Spanish authorities reported a confirmed case of EVD in a healthcare worker who participated in the medical care of the second Spanish patient repatriated to Spain with Ebola infection. The medically evacuated patient arrived in Spain on 22 September and died on 25 September. The infected healthcare worker represents the first transmission of Ebola infection outside of West Africa region [48].

The healthcare worker is a woman working in La Paz-Carlos III hospital in Madrid. She reportedly developed fever the night of 29 September. According to the Spanish Ministry of Health, she participated in the medical care of the repatriated patient and was wearing appropriate personal protection equipment (PPE). Her tasks did not include

medical procedures. As part of the protocol, she performed self-monitoring and was to contact occupational health services if she developed fever or other symptoms.

The nurse is reported to have entered the EVD patient's room twice, once when the patient case was alive and once after his death. Preliminary results of the investigation point to an incident during the removal of the PPE on 24 September as the mode of transmission.

She was admitted to La Paz-Carlos III Hospital on 6 October and is under strict isolation [49].

The Spanish authorities have initiated contact tracing and, as of 10 October, 72 contacts, of which 13 are considered as high-risk contacts, are being actively monitored. Quarantine has been established or is under assessment for high-risk contacts.

Medical evacuations and repatriations from EVD-affected countries

Seventeen individuals have been evacuated or repatriated from the EVD-affected countries (Table 3, Figure 4).

As of 13 October, nine medical evacuations of confirmed EVD cases to Europe have taken place (three in Germany, two in Spain, one in the UK, one in France, one in Norway and one in Switzerland) as well as two repatriations of exposed persons to the Netherlands.

Date of evacuation (in 2014)	Evacuated from	Evacuated to	Profession	Status	Confirmed	Citizenship
2 August 2014	Liberia	Atlanta (USA)	Healthcare worker	Discharged	Yes	USA
5 August 2014	Liberia	Atlanta (USA)	Healthcare worker	Discharged	Yes	USA
6 August 2014	Liberia	Madrid (Spain)	Healthcare worker	Death	Yes	Spain
24 August 2014	Sierra Leone	London (United Kingdom)	Healthcare worker	Discharged	Yes	UK
27 August 2014	Sierra Leone	Hamburg (Germany)	Epidemiologist	Recovered	Yes	Senegal
4 September 2014	Monrovia, Liberia	Omaha (USA)	Physician (obstetrician)	Stable	Yes	USA
9 September 2014	Kenema, Sierra Leone	Atlanta (USA)	Physician	Stable	Yes	USA
14 September 2014	Sierra Leone	Leiden (the Netherlands)	Healthcare worker	Discharged	No	the Netherlands
14 September 2014	Sierra Leone	Leiden (the Netherlands)	Healthcare worker	Discharged	No	the Netherlands
19 September 2014	Liberia	Paris (France)	Healthcare worker	Discharged	Yes	France
22 September 2014	Sierra Leone	Madrid (Spain)	Healthcare worker	Death	Yes	Spain
22 September 2014	Sierra Leone	Lausanne (Switzerland)	Healthcare worker	Admitted	Unknown	Non-Swiss
28 September 2014	Sierra Leone	Maryland (USA)	Healthcare worker	Admitted	Unknown	USA
2 October 2014	Sierra Leone	Frankfurt (Germany)	Healthcare worker	Stable	Yes	Uganda
2 October 2014	Liberia	Omaha (USA)	Cameraman	Stable	Yes	USA
6 October 2014	Sierra Leone	Oslo (Norway)	Healthcare worker	Unknown	Yes	Norway
8 October 2014	Liberia	Leipzig (Germany)	Laboratory worker	Death	Yes	Sudan

Table 3. Medical evacuation and repatriation from EVD-affected countries up to 13 October 2014



Figure 4. Medical evacuation and repatriations from EVD-affected countries, as of 13 October 2014

ECDC threat assessment

With nearly 9 000 cases and more than 4 000 deaths reported from West Africa by mid-October 2014, it is clear that the control measures implemented so far have failed to control the outbreak. All evidence and predictions indicate that the epidemic will continue to increase and spread geographically in affected countries if control efforts remain unchanged.

The clinical course of the disease and the estimated transmissibility of the virus are similar to previous EVD outbreaks. Current knowledge does not indicate that this unprecedented outbreak results from increased pathogenicity of the outbreak strain of Ebola virus [38]. As in earlier EVD outbreaks, transmission seems to be primarily driven by direct contact with EVD cases and dead bodies. There is no convincing evidence that the recommended infection control measures are inappropriate to ensure protection if adhered to strictly by trained staff working in health services with appropriate facilities.

As a consequence, the aim of the Ebola outbreak response in the affected countries is to interrupt chains of human-to-human transmission based on the following activities:

- To quickly identify and isolate suspected EVD cases for laboratory confirmation and supportive treatment in isolation wards.
- To ensure safe removal and burial of deceased EVD cases.
- To identify all contacts of each EVD case, actively monitor their health for the maximum incubation period of 21 days, and isolate, diagnose and treat all contacts who develop symptoms.
- To minimise the risk of transmission in healthcare settings through the consistent and appropriate use of PPE and handling of hospital waste.
- To instruct community leaders about the disease, ways of transmission and how to protect against infection, and to engage them in communicating this information to community members.
- To raise public awareness and promote adherence to protective behaviour [23,50].

The current outbreak amplitude challenges response activities and requires a large international effort to enhance healthcare services and infection control measures, ensure supply of protective equipment in treatment facilities

and strengthen and support capacities for epidemiological surveillance and laboratory diagnosis. Beyond the public health emergency, the current crisis of unprecedented scale is a threat to healthcare systems with an impact on standard medical care for other pathologies. In the most affected countries, others sectors are suffering, notably economic sectors and food security making this crisis an international and complex health emergency requiring a large-scale multi-sectorial response [51,52].

If the outbreak continues with the current dynamics, without effective measures in place, a potentially explosive evolution is expected, with serious consequences for the region. The risk of importation to the EU is linked to the magnitude of the outbreak in West Africa and further stresses the need to efficiently control the outbreak there.

Risk of exposure to EU residents and travellers in West African affected countries

Exposure in the community

- The risk of infection for EU residents and visitors in the affected countries through exposure in the community
 is considered low if they adhere to the recommended precautions. The upsurge in the number of new EVD
 cases over the last weeks, the existence of urban transmission, and the fact that not all chains of transmission
 are known, increase the likelihood that residents and travellers to the EVD-affected countries will be exposed
 to infected or ill persons.
- People visiting friends and relatives in the affected countries tend to have more and closer contacts in the community, and they are more likely to be at risk than other visitors, particularly if they care for sick friends and relatives or participate in burial ceremonies –activities known to be associated with transmission of the Ebola viruses.

Exposure in healthcare settings

- Residents and visitors to the affected areas run a risk of exposure to EVD in healthcare facilities. The level of
 this risk is related to how well the infection control measures are being implemented in these settings and the
 nature of the care required.
- The risk of exposure in healthcare settings also exists in areas that have not yet reported cases because it can be assumed that not all cases of EVD are immediately detected and reported.
- The infection risk is not limited to hospitals that provide care to known EVD cases because infectious cases may initially seek medical attention at any healthcare provider.
- While the risk is low for a consultation requiring non-invasive tests and prescription of oral drugs to patients
 who do not have severe symptoms such as profuse diarrhoea or haemorrhage, it may be increased if invasive
 procedures are required.
- The risk of being exposed to Ebola viruses is obviously higher for healthcare workers and volunteers who
 provide assistance in settings where no infection control measures have been implemented. The risk is
 extremely high for healthcare workers who carry out invasive medical procedures or provide care to EVD
 patients without proper infection control measures and PPE [53].

Risk of importation to the EU

General assessment

It is expected that the number of new cases will continue to rise in Guinea, Liberia and Sierra Leone in the coming weeks and possibly months [6]. Therefore, the likelihood of individuals arriving in the EU with potential Ebola virus infection has increased since the previous assessments were made.

People infected with EVD may arrive in the EU by direct or indirect flights from affected countries or on board freighters or passenger ships:

- They may arrive while incubating the disease. These persons do not show symptoms and cannot be detected through screening at points of exit or entry.
- They may arrive sick because they developed symptoms while travelling.

Almost all EU/EEA countries have issued temporary travel advice against non-essential travel to EVD-affected countries. A number of international airlines have stopped or substantially reduced the number of flights to the three most affected countries in West Africa.

A remote possibility is a chain of transmission along the routes used by undocumented migrants who end up on the southern shore of the Mediterranean and attempt to reach Europe by sea. Although the probability of this event is very small, the consequences of an outbreak in a detention centre or on board ship at sea could be dramatic.

The international response continues to be scaled up with involvement of UN agencies, international organisations, non-governmental and governmental actors [54]. The number of EU citizens involved in the response is expected to increase with the progressive deployment of EU support to outbreak response activities in affected countries. In general, the standards of infection control and personal protection measures must be strictly maintained in order to minimise the exposure of care givers to Ebola virus and the need for repatriation or medical evacuation of healthcare workers and volunteers. There has been a recent increase in reports of expatriate healthcare workers being repatriated or medically evacuated from EVD-affected countries following exposure or infection with Ebola virus (Table 3). The need for repatriations and medical evacuations will increase as the epidemic continues to grow and more international staff are engaged in the response. It is likely that the crisis will continue for several months and the probability of unplanned importations (non-medical evacuations) of Ebola virus to the EU will increase over time as the epidemic spreads.

Patients presenting with symptoms and seeking medical attention in the EU

There is a possibility that a person who was exposed to Ebola virus develops symptoms while on a commercial flight. It is expected that such patients would be detected and reported to a healthcare facility upon arrival in the EU and then be isolated to reduce the risk of further transmission.

Travel and transport risk assessment

A traveller on board an airplane may be already ill or become ill during the flight, showing symptoms compatible with EVD. In this situation, the possibility of transmission to co-passengers and crew should be assessed using the ECDC RAGIDA guidelines [55].

If an investigation concludes that the passenger has symptoms compatible with EVD and was exposed to EVD in the past 21 days, all passengers and crew who report direct contact, as well as all passengers seated one seat away from the sick person, should be monitored for 21 days. In addition, all passengers, crew members and cleaning staff who had direct contact with the suspected case's bodily fluids or potentially contaminated fomites such as contaminated clothing, towels, or other utensils, should be investigated and monitored.

Any person who was exposed to Ebola viruses and develops symptoms while on board a freighter/passenger ship sailing to the EU should be declared in a Maritime Declaration of Health form and in accordance with article 37 of the 2005 International Health Regulations [56]. Affected crew members or passengers should be taken care of appropriately in order to prevent further spread of the disease.

Risk related to biosafety

There is a theoretical risk that a biological sample is sent to an EU laboratory for further testing, without proper indication of a possible connection to Ebola virus. Strict compliance with sample shipment regulations and universal precautions in the receiving laboratory should mitigate this risk [57].

Risk of transmission through substances of human origin

According to the EU Blood Directive [58], current geographic deferrals for malaria also exclude residents and travellers from EVD-affected countries from donating blood. An ECDC technical report assessing the risk of Ebola virus transmission through substances of human origin was published on the 6 October 2014. The document offers guidelines on the safety of donations where the potential donors are travellers returning from Ebola-affected countries, people exposed to Ebola virus and patients who have recovered from the disease [59].

Risk of Ebola virus transmission in the EU following importation

The probability of sustained chains of EVD transmission in the EU is low due to the high capacity of Member States to identify suspected cases, perform laboratory testing, isolate and treat EVD patients, and to conduct contact tracing. Recent reports from Spain and Dallas indicate, however, that there is no place for complacency about the risks of healthcare-associated transmission unless infection control measures are strictly and assiduously applied and followed.

Repatriation and medical evacuation

The risk of Ebola virus spreading from an EVD patient who arrives in the EU as result of a planned medical evacuation is considered to be low when appropriate measures are strictly adhered to, but cannot be excluded in exceptional circumstances. The risk associated with an asymptomatic person who is repatriated following a low-risk exposure to Ebola virus in the affected area is equally low.

Individuals seeking medical care in the EU

EVD cases may travel during the incubation period and therefore not present with symptoms at the time of departure from affected countries or arrival in the EU. Once in the EU, detection may be delayed when either symptomatic persons are unaware of exposure or deny it, or, when presenting to an EU healthcare facility, clinicians do not suspect EVD.

The infectiousness of EVD patients is low at the early prodromal stages of the disease and increases as the disease progresses and the viral load increases. Infectiousness becomes particularly high when symptoms include the dissemination of infected bodily fluids, e.g. when vomiting, experiencing diarrhoea or bleeding.

The risk of unprotected contact is high during the period from the start of symptoms until the EVD-infected individual seeks medical care. The risk still exists in healthcare settings during the initial ascertainment until precautions to prevent transmission are fully and appropriately implemented [60,61].

Therefore, secondary transmission to caregivers in the family and in healthcare facilities can occur, particularly through exposure to bodily fluids (bleeding, diarrhoea) before an Ebola virus infection is suspected and appropriate infection control measures have been implemented.

The periods most at risk of secondary transmission include early and late stages of the disease:

- Early stage of the disease, when patients are not yet very contagious, but unprotected contacts are occurring.
- Late stage of the disease, after EVD is confirmed, when patients may experience very high viral loads while undergoing contamination-prone invasive procedure in intensive care units.

Delays in recognition of EVD as the cause of symptomatic disease can result in a significant risk of transmission if infection control measures are not taken during the period between symptom onset and recognition of EVD as the suspected or confirmed cause of disease. Once a case is detected and appropriate Ebola infection control measures are implemented, the risk of transmission becomes very low if those measures are fully adhered to, including assiduous care with respect to the donning and removal of PPE. Interventions aimed at reducing the risk of spread from an imported case in the EU should therefore focus on narrowing the window from onset of symptoms to implementation of effective infection control measures and ensuring that those infection control measures are strictly adhered to.

The case who recently developed the disease in Dallas, Texas, after arriving from Liberia, reminds us of the possibility of a similar situation occurring in the EU. In this situation, reduction of the risk of EVD secondary transmission to close contacts depends on early detection of suspected cases by healthcare professionals, rapid laboratory confirmation of infection and early isolation of the patient following onset of symptoms.

The ongoing investigation in Spain will provide information to further understand how the infection was transmitted to this healthcare worker. There is currently no evidence that the transmission to the healthcare worker may have resulted from a change in the transmissibility of the virus [38]. Therefore, the recommended infection control measures remain appropriate to ensure protection, if strictly applied.

Following the detection of EVD cases in the EU, the interruption of all chains of human-to-human transmission is of the highest priority. This can be achieved by:

- quickly identifying and isolating suspected EVD cases for confirmation by laboratory diagnosis and supportive treatment in an isolation ward; and
- identifying all contacts of each EVD case, including healthcare workers involved the patient's care, monitoring (actively or passively depending on risk) their health for the maximum incubation period of 21 days, and offering immediate care, isolation and laboratory diagnosis to all contacts that develop symptoms.

Options for risk reduction

The focus of this document is on individual protection and the various options for mitigating the risk of importation and spread in the EU.

Reduction of the risk of infection in West Africa

Avoiding travel to affected areas

The most obvious option to decrease the risk of importation from affected areas is to advise travellers to defer their travel to affected countries or areas until the outbreak is controlled there. Thirty EU/EEA countries have recommended this option for their citizens. Twenty-six are currently recommending that non-essential travel should be avoided or postponed, and four advise against all travel in the affected areas. The World Health Organization does not recommend any travel or trade restrictions to countries involved in this outbreak [62].

Preventing infection in communities

Visitors and residents in EVD-affected areas face a low risk of becoming infected in the community if the following precautions are strictly followed:

- Avoid contact with symptomatic patients and their bodily fluids.
- Avoid contact with corpses and/or bodily fluids from deceased patients.
- Avoid contact with wild animals (including primates, monkeys, forest antelopes, rodents and bats), both alive and dead, and consumption of bushmeat.
- Wash hands regularly, using soap or antiseptics.

Generic precautions for travelling in West African countries also apply to the prevention of EVD infection:

- Wash and peel fruit and vegetables before consumption.
- Avoid unprotected sexual intercourse.
- Avoid habitats which might be populated by bats, such as caves, isolated shelters or mining sites.

Preventing infection in healthcare settings

There is an increased risk of exposure and infection in healthcare facilities. Options for prevention and control of this risk include:

- Avoid non-essential travel to EVD-affected areas and countries.
- Identify appropriate in-country healthcare resources in the EVD-affected countries prior to travelling there.
- Ensure that your travel insurance covers medical evacuation in the event of illness or accident in order to limit exposure to local health facilities.

However, recent events in the affected countries have demonstrated that it may not always be possible to comply with the above precautions and this is the rationale behind many countries' advice against non-essential travel to affected countries.

Reduction of the risk of importation to the EU

Options in affected countries

Following the declaration of the Public Health Event of International Concern (PHEIC) on 8 August 2014, WHO recommended the following measures for affected Member States, which are expected, if implemented efficiently, to reduce the risk for importation to the EU:

- Affected countries are requested to conduct exit screening of all persons at international airports, seaports and major land crossings for unexplained febrile illness consistent with potential Ebola infection.
- There should be no international travel of known Ebola cases or contacts of cases, unless the travel is part of an appropriate medical evacuation. To be fully effective, this measure should restrict asymptomatic contacts of EVD cases from leaving the EVD-affected country on an international flight until the 21-day incubation period has passed. As the ratio of contacts to cases is high, this measure represents a significant logistical challenge. It may also prevent expatriate professionals engaged in outbreak control from leaving the EVD-affected country if they have been exposed to Ebola viruses.

Exit screening could potentially prevent a febrile EVD case from boarding a flight but it would not detect an incubating passenger who has not yet developed fever [63]. Information about exit screening in the affected countries will remain of interest in order to monitor the risk of importation of potential EVD cases to non-affected countries.

Options for EU countries

Screening of travellers

The following section is adapted from the summary of the ECDC document on screening [64].

As the epidemic of Ebola virus disease (EVD) continues to rise in West Africa, there is an increasing possibility that infected individuals will travel to the EU.

Exit screening focuses efforts on those at highest risk, thereby minimising the resources required and maximising the positive predictive value of screening. Affected countries have implemented exit screening, supported by the US Centers for Disease Control and Prevention (CDC). Based on current estimates of prevalence of infection (2 per 10 000 population in the affected countries) and what was observed during the first two months of exit screening in the three affected countries, the predictive positive value of the detection of one individual through screening is extremely low, as no EVD was confirmed in the 77 who were detected out of 36 000 travellers screened.

Entry screening to non-affected countries is being considered, or has been adopted, by a small number of countries, in addition to the ongoing exit screening. Based on the evidence of the validity of methods currently available for entry screening at major points of entry, and the likely prevalence of screening-detectable cases among those who have undergone exit screening, the added value of entry screening, if exit screening is being conducted effectively, is likely to be very small, and the resource implications considerable.

Complementing exit screening with entry screening may, however, be considered:

- When there are doubts about the efficiency of exit screening
- To detect the few who may develop fever between the time of departure and the time of arrival. This could be considered in particular for long haul flights with multiple connections, extending beyond 12 hours.

The following points need to be considered in order to support decision-making by EU public health authorities:

- No information is currently available regarding the quality and performance of the exit screening implemented in the affected countries.
- The use of screening for infectious diseases has not proven to be effective to prevent or delay transmission in past epidemics such as SARS.
- Temperature screening of passengers is able to detect travellers presenting with high fever with an appropriate level of performance when using appropriate equipment operated by trained staff.
- Temperature screening requires protocols and resources to further investigate possibly febrile passengers detected in order to perform appropriately.
- Screening will result in a significant increase in the request for Ebola testing.
- Even the best temperature screening scheme will:
 - miss up to 20% of the febrile symptomatic EVD cases (sensitivity of the measurement)
 - miss travellers concealing their fever
 - miss two-thirds of infected cases, still incubating and not yet presenting with symptoms
 - detect cases of fever related to many different infectious diseases such as malaria or influenza; it is likely that EVD cases will account for an extremely small proportion of febrile passengers, if any.
- Complementing temperature screening with visual review and a health questionnaire may be considered:
 - to increase the performance of screening relying only on temperature screening
 - to identify possibly contagious travellers missed by temperature screening
 - to identify travellers having had high-risk exposure and enrol them in monitoring schemes or quarantine.

Overall, screening for EVD among travellers may detect a few contagious EVD cases over time. Given that there is no available evidence of the effectiveness of exit screening in the affected countries, entry screening remains an option to be considered, in particular for direct flights, despite its low yield and high investment, to contribute to the prevention of importation of the disease.

Travel restrictions and screening of passengers on arrival (entry screening) at sea ports, airports or ground crossings in non-affected countries that do not share borders with affected countries are not currently recommended by WHO [63].

Reduction of the risk of transmission within the EU following an importation

The risk of EVD transmission in the EU can be reduced by the early detection of suspected EVD cases imported into the EU and the use of appropriate infection control measures. Interventions aiming to reduce the risk of transmission within the EU include the following options:

Investigation of possible cases

The time window between the onset of first symptoms and the detection by healthcare systems should be minimised. Investigation of individuals who present to healthcare providers with EVD-like symptoms and meet the criteria for 'persons under investigation'^{*} should be swiftly and safely conducted in order to allow timely detection of EVD cases. In addition, investigations should consider other possible aetiologies of febrile illness upon return from tropical areas, with priority given to malaria, even though malaria positivity does not exclude an EVD infection. It is expected that a significant number of people will be tested for EVD in the EU/EEA, but the likelihood of identifying and confirming an EVD case is low (low positive predictive value) and other infections will be identified.

Contact tracing

After identification and management of confirmed and/or probable EVD case(s) and potential chains of transmission in EU, effective contact tracing and contact management should reduce the risk of spread of EVD in the EU. The aim is to identify all contacts of each EVD case, assess their level of exposure, actively monitor their health for the maximum incubation period of 21 days, and isolate, diagnose and treat all contacts who develop symptoms.

Medical evacuations

There are increasingly frequent reports about expatriate healthcare workers being repatriated from EVD-affected countries for monitoring after exposure to Ebola viruses. Such repatriations should be executed as soon as possible after the potential exposure, while the risk of transmission is still minimal should the exposed person turn out to be infected.

A document entitled 'Assessment and planning for medical evacuation by air to the EU of patients with Ebola virus disease and people exposed to Ebola virus' provides decision-makers with additional information when there is a perceived need to evacuate by air an infected or exposed person from an Ebola-affected country to an EU Member State [65]. The decision to evacuate must be based on: the likelihood of the person being infected with Ebola virus; the potential benefits of evacuation for the concerned person/patient; the risks associated with medical evacuation by air for the person/patient; and the risk of transmission to the crew and accompanying medical staff.

It is anticipated that medical evacuation needs will grow over the coming months as the outbreak continues and the number of expatriate healthcare workers engaged in outbreak control increases.

Healthcare settings

Transmission to healthcare workers can be prevented by the strict application of infection control measures as recommended by WHO [25]. However, even when infection control measures are thoroughly applied, transmission to healthcare workers can still exceptionally occur. Infection of a healthcare worker may result from a breach in the strict application of the infection control measures, when caring for an infectious patient, when involved in waste management or when removing PPE.

The early detection and isolation of a patient with EVD decreases the risk of transmission in the community. However, care in the hospital setting especially when aerosol-generating procedures are performed during the late stages of the disease when patients are highly contagious, implies a risk to healthcare practitioners. Minimising this risk constitutes an essential target.

^{*} European Centre for Diseases Prevention and Control. Ebola virus disease case definition for reporting in the EU. http://ecdc.europa.eu/en/healthtopics/ebola_marburg_fevers/EVDcasedefinition/Pages/default.aspx

According to WHO guidelines [53] the following are essential for the safe medical care of EVD patients:

- Isolation rooms with dedicated bathroom
- Availability of personal protection equipment
- Personnel adequately trained to use the equipment.

Tools that need to be considered for the optimisation of the safe management of patients include regularly repeated hands-on training in the use of PPE, the performance of simulation exercises, continuous supervision and monitoring of both the care of the patient and the putting on and removal of PPE and working in pairs (buddy system). Transfer of the patient to a specialised high-level isolation unit is an option that may be considered, taking into account availability, feasibility and the safety of transfer.

An enhanced occupational health policy with active monitoring of staff who have been involved in the care of EVD patients would ensure the early detection, isolation and treatment of secondary cases among healthcare workers. Such policies should also consider psychosocial support of healthcare workers. The possibility of restricting the number of contacts and recording contacts (e.g. contact diary) during the 21 days following the last exposure may be considered, particularly for a case of high-risk exposure.

Information and communication

Raising awareness among returning travellers from affected areas or any person having had a contact with probable or confirmed cases about disease symptoms and appropriate actions (self-isolation and seeking medical care mentioning potential exposure) should be considered to reduce the time between the onset of illness and isolation, in order to reduce the opportunity for further transmission to other persons and the generation of new chains of transmission.

The following are considered:

- Informing travellers departing from EVD-affected countries and travellers arriving in the EU on direct flights from EVD-affected countries about:
 - the possibility of exposure to Ebola while in the affected countries
 - the clinical presentation of the disease and the need to seek immediate medical care if symptoms develop
 - the need to immediately disclose their travel history when seeking medical care, and to preferably do so before arriving at a healthcare facility
 - the need to indicate possible contact with sick individuals or wild animals while in the EVD-affected country
 - how to contact public health authorities for support if infection is suspected (leaflets, phone numbers, telephone hotline).
- Informing and sensitising healthcare providers in the EU about:
 - the possibility of EVD among returning travellers from affected areas
 - the clinical presentation of the disease and the need to inquire about travel history and contacts with family and friends visiting from EVD-affected countries
 - the availability of protocols for the ascertainment of possible cases and procedures for referral to healthcare facilities
 - the imperative need for strict implementation of barrier management, use of personal protective equipment and disinfection procedures, in accordance with specific guidelines and WHO infection control recommendations when providing care to suspected EVD cases [26,53]
 - provide training before caring for EVD patients and support staff during their duties (e.g. stress management).
- Supporting healthcare providers in the EU with resources that will help them to identify and manage potential EVD patients:
 - Assessing and planning medical evacuation by air to the EU for patients with Ebola virus disease and people exposed to Ebola virus [65]
 - Case definitions for Ebola patients in the EU [66]
 - <u>Case identification algorithm [61]</u>
 - <u>Case management algorithm [60]</u>

References

1. European Centre for Disease Prevention and Control. Outbreak of Ebola haemorrhagic fever in Guinea - rapid risk assessment. 23 March 2014. [Internet]. Stockholm: ECDC; 2014. Available from: http://ecdc.europa.eu/en/publications/Publications/ebola-guinea-rapid-risk-assessment.pdf.

2. European Centre for Disease Prevention and Control. Outbreak of Ebola virus disease in West Africa - rapid risk assessment. 8 April 2014 [Internet]. Stockholm: ECDC; 2014. Available from:

http://www.ecdc.europa.eu/en/publications/Publications/Ebola-RRA-West-Africa-8April2014.pdf.

3. European Centre for Disease Prevention and Control. Outbreak of Ebola virus disease in West Africa - rapid risk assessment. Second update, 9 June 2014 [Internet]. Stockholm: ECDC; 2014. Available from: http://www.ecdc.europa.eu/en/publications/Publications/ebola-risk-assessment-virus-Guinea-Liberia-Sierra-Leone.pdf.

4. European Centre for Disease Prevention and Control. Outbreak of Ebola virus disease in West Africa - rapid risk assessment. Third update, 1 August 2014. [Internet]. Stockholm: ECDC; 2014. Available from: http://www.ecdc.europa.eu/en/publications/Publications/ebola-outbreak-west-africa-1-august-2014.pdf.

5. European Centre for Disease Prevention and Control. Outbreak of Ebola virus disease in West Africa - rapid risk assessment. Fourth update, 3 September 2014. [Internet]. Stockholm: ECDC; 2014. Available from: http://www.ecdc.europa.eu/en/publications/Publications/Ebola-virus-disease-west-africa-risk-assessment-27-08-2014.pdf.

6. European Centre for Disease Prevention and Control. Outbreak of Ebola virus disease in West Africa - rapid risk assessment. Fifth update, 29 September 2014 [Internet]. Stockholm: ECDC; 2014. Available from: http://ecdc.europa.eu/en/publications/Publications/Ebola-Sierra%20Leone-Liberia-Guinea-Nigeria-23-09-2014-rapid-risk-assessment.pdf.

7. European Centre for Disease Prevention and Control. Outbreak of Ebola virus disease in West Africa - rapid risk assessment. Sixth update, 13 October 2014 [Internet]. Stockholm: ECDC; 2014. Available from: http://ecdc.europa.eu/en/publications/Publications/ebola-sierra-leone-liberia-guinea-nigeria-spain-14-10-2014-risk-assessment.pdf.

8. European Centre for Disease Prevention and Control. Ebola and Marburg fevers - factsheet [Internet]. Stockholm: ECDC; 2014 [cited 2014 Oct 8]. Available from:

http://www.ecdc.europa.eu/en/healthtopics/ebola_marburg_fevers/pages/index.aspx.

9. Li YH, Chen SP. Evolutionary history of Ebola virus. Epidemiol Infect. 2014 Jun;142(6):1138-45.

10. United Nations Office for the Coordination of Humanitarian Affairs Democratic Republic of Congo. Update in the Ebola virus disease in DRC. No. 5. [Internet]. OCHA; 2014 [updated Aug 30 2014; cited 2014 Aug 30]. Available from: <u>http://www.rdc-</u>

humanitaire.net/attachments/article/4924/Ebola%20Update%20of%2030%20August%202014%20-%20No%205%20ENG.pdf.

11. Piercy TJ, Smither SJ, Steward JA, Eastaugh L, Lever MS. The survival of filoviruses in liquids, on solid substrates and in a dynamic aerosol. J Appl Microbiol. 2010 Nov;109(5):1531-9.

12. Public Health Agency of Canada. Ebola virus. Pathogen Safety Data Sheet - Infectious substances [Internet]. Public Health Agency of Canada.; 2014 [updated 2014 Aug; cited 2014 Oct 8]. Available from: http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/ebola-eng.php.

13. Centers for Disease Control and Prevention. Interim guidance for environmental infection control in hospitals for Ebola virus [Internet]. Atlanta: CDC; 2014 [updated 2014 Oct 3; cited 2014 Oct 7]. Available from: http://www.cdc.gov/vhf/ebola/hcp/environmental-infection-control-in-hospitals.html.

14. Chepurnov AA, Chuev Iu P, P'Iankov O V, Efimova IV. [The effect of some physical and chemical factors on inactivation of the Ebola virus]. Vopr Virusol. 1995 Mar-Apr;40(2):74-6.

15. World Health Organization. A Guide for Shippers of Infectious Substances [Internet]. Geneva: WHO; 2013 [cited 2014 Oct 8]. Available from: <u>http://www.who.int/ihr/infectious_substances/en/</u>.

16. Bannister B. Viral haemorrhagic fevers imported into non-endemic countries: risk assessment and management. Br Med Bull. 2010;95:193-225.

17. Bausch DG, Towner JS, Dowell SF, Kaducu F, Lukwiya M, Sanchez A, et al. Assessment of the risk of Ebola virus transmission from bodily fluids and fomites. J Infect Dis. 2007 Nov 15;196 Suppl 2:S142-7.

18. Colebunders R, Borchert M. Ebola haemorrhagic fever - a review. J Infect. 2000 Jan;40(1):16-20.

19. World Health Organization. What we know about transmission of the Ebola virus among humans. Ebola situation assessment. 6 October 2014. [Internet]. Geneva: WHO; 2014 [cited 2014 Oct 6]. Available from: http://www.who.int/mediacentre/news/ebola/06-october-2014/en/.

20. Dowell SF, Mukunu R, Ksiazek TG, Khan AS, Rollin PE, Peters CJ. Transmission of Ebola hemorrhagic fever: a study of risk factors in family members, Kikwit, Democratic Republic of the Congo, 1995. J Infect Dis. 1999 Feb;179 Suppl 1:S87-91.

21. Ksiazek TG, Rollin PE, Williams AJ, Bressler DS, Martin ML, Swanepoel R, et al. Clinical virology of Ebola hemorrhagic fever (EHF): virus, virus antigen, and IgG and IgM antibody findings among EHF patients in Kikwit, Democratic Republic of the Congo, 1995. J Infect Dis. 1999 Feb;179 Suppl 1:S177-87.

22. Towner JS, Rollin PE, Bausch DG, Sanchez A, Crary SM, Vincent M, et al. Rapid diagnosis of Ebola hemorrhagic fever by reverse transcription-PCR in an outbreak setting and assessment of patient viral load as a predictor of outcome. J Virol. 2004 Apr;78(8):4330-41.

23. World Health Organization. Ebola virus disease – fact sheet No 103. [Internet]. Geneva: WHO; 2014 [updated 2014 Sep; cited 2014 Oct 8]. Available from: <u>http://www.who.int/mediacentre/factsheets/fs103/en/</u>.

24. Rowe AK, Bertolli J, Khan AS, Mukunu R, Muyembe-Tamfum JJ, Bressler D, et al. Clinical, virologic, and immunologic follow-up of convalescent Ebola hemorrhagic fever patients and their household contacts, Kikwit, Democratic Republic of the Congo. Commission de Lutte contre les Epidemies a Kikwit. J Infect Dis. 1999 Feb;179 Suppl 1:S28-35.

25. Martini GA, Schmidt HA. [Spermatogenic transmission of the "Marburg virus". (Causes of 'Marburg simian disease')]. Klin Wochenschr. 1968 Apr 1;46(7):398-400.

26. World Health Organization. Clinical management of patients with viral haemorrhagic fever: a pocket guide for the front-line health worker. 30 March 2014 [Internet]. Geneva: WHO; 2014. Available from: http://apps.who.int/iris/bitstream/10665/130883/2/WHO HSE PED AIP 14.05.pdf?ua=1.

27. World Health Organization. Potential Ebola therapies and vaccines (background document for participants of the WHO Consultation on potential Ebola therapies and vaccines in Sep 2014) [Internet]. WHO; 2014 Sep 3 [cited 2014 Oct 8]. Available from: <u>http://www.who.int/csr/disease/ebola/ebola-new-interventions-02-sep-2014.pdf?ua=1</u>.

28. Friedrich BM, Trefry JC, Biggins JE, Hensley LE, Honko AN, Smith DR, et al. Potential vaccines and postexposure treatments for filovirus infections. Viruses. 2012 Sep;4(9):1619-50.

29. World Health Organization. Statement on the WHO consultation on potential Ebola therapies and vaccines [Internet]. Geneva: WHO; 2014 [cited 2014 Oct 8]. Available from:

http://www.who.int/mediacentre/news/statements/2014/ebola-therapies-consultation/en/.

30. European Medicines Agency. Ebola outbreak: EMA to review experimental medicines to support treatment decisions [Internet]. London: EMA; 2014 [cited 2014 Oct 8]. Available from:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news and events/news/2014/09/news detail 002176.jsp& mid=WC0b01ac058004d5c1.

31. World Health Organization. Disease outbreak news: Ebola virus disease in Guinea [Internet]. Geneva: WHO; 2014 Mar 23 [cited 2014 Oct 8]. Available from: <u>http://www.who.int/csr/don/2014_03_23_ebola/en/</u>.

32. Baize S, Pannetier D, Oestereich L, Rieger T, Koivogui L, Magassouba NF, et al. Emergence of Zaire Ebola virus disease in Guinea. N Engl J Med. 2014;371(15):1418-25.

33. Muyembe-Tamfum JJ, Mulangu S, Masumu J, Kayembe JM, Kemp A, Paweska JT. Ebola virus outbreaks in Africa: past and present. Onderstepoort J Vet Res. 2012;79(2):451.

34. Centers for Disease Control and Prevention. Traveler's health: Ebola in Liberia [Internet]. Atlanta: CDC; 2014 [updated 2014 Oct 7; cited 2014 Oct 14]. Available from: <u>http://wwwnc.cdc.gov/travel/notices/alert/ebola-liberia</u>.

35. Centers for Disease Control and Prevention. Traveler's health: Ebola in Sierra Leone [Internet]. Atlanta: CDC; 2014 [updated 2014 Oct 7; cited 2014 Oct 13]. Available from:

http://wwwnc.cdc.gov/travel/notices/alert/ebola-sierra-leone.

36. World Health Organization. WHO statement on the meeting of the International Health Regulations Emergency Committee regarding the 2014 Ebola outbreak in West Africa [Internet]. Geneva: WHO; 2014 [cited 2014 Aug 29]. Available from: <u>http://who.int/mediacentre/news/statements/2014/ebola-20140808/en/</u>.

37. United Nations Security Council. Resolution 2177 (2014). Adopted by the Security Council at its 7268th meeting on 18 September 2014 [Internet]: UN; 2014 [cited 2014 Oct 8]. Available from: http://www.ifrc.org/docs/IDRL/UN%20SC%20Res.pdf.

38. WHO Ebola Response Team. Ebola Virus Disease in West Africa - The First 9 Months of the Epidemic and Forward Projections. N Engl J Med. 2014 Oct 16;371(16):1481-95.

39. Texas Department of State Health Services. Texas patient tests positive for Ebola [Internet]. Texas Department of State Health Services; 2014 Oct 10 [cited 2014 Oct 11]. Available from: https://www.dshs.state.tx.us/. 40. World Health Organization. Ebola response roadmap situation report. 15 October 2014 [Internet]. Geneva: WHO; 2014. Available from:

http://apps.who.int/iris/bitstream/10665/136508/1/roadmapsitrep15Oct2014.pdf?ua=1.

41. World Health Organization. Ebola response roadmap situation report. 1 October 2014 [Internet]. Geneva: WHO; 2014. Available from:

http://apps.who.int/iris/bitstream/10665/135600/1/roadmapsitrep 1Oct2014 eng.pdf?ua=1.

42. World Health Organization. Ebola response roadmap situation report. 8 October 2014. [Internet]. Geneva: WHO; 2014. Available from:

http://apps.who.int/iris/bitstream/10665/136020/1/roadmapsitrep_80ct2014_eng.pdf?ua=1.

43. Médecins Sans Frontières Espagne. La realidad trágica de los que trabajan en Ebola [in Spanish - The tragic reality of working with Ebola] [Internet]. Barcelona: MSF; 2014 Sep 26 [cited 2014 Oct 16]. Available from: http://www.msf.es/noticia/2014/realidad-tragica-que-trabajan-en-ebola

44. Centers for Disease Control and Prevention. Cases of Ebola diagnosed in the United States [Internet]. Atlanta: CDC; 2014 [cited 2014 Oct 8]. Available from: <u>http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/united-states-imported-case.html#ebola-contact-tracing</u>.

45. Centers for Disease Control and Prevention. Texas reports positive test for Ebola in one additional healthcare worker [Internet]. Atlanta: CDC; 2014 Oct 15 [cited 2014 Oct 16]. Available from: http://www.cdc.gov/media/releases/2014/s1015-texas-second-health-care-worker.html.

46. CBS DFW. 3rd Dallas Ebola patient arrives at Emory hospital in Atlanta [Internet]. CBS DFW; 2014 Oct 15 [cited 2014 Oct 16]. Available from: <u>http://dfw.cbslocal.com/2014/10/15/3rd-dallas-ebola-patient-headed-to-emory-university-hospital/</u>.

47. Ribner BS. Lessons learned treating Ebola patients in US [video] [Internet]. Healio Infectious Disease News; 2014 Oct 8 [cited 2014 Oct 16]. Available from: <u>http://www.healio.com/infectious-disease/practice-management/news/online/%7B443af8d6-a116-4071-9c72-a743bc1ff078%7D/lessons-learned-treating-ebola-patients-in-us.</u>

48. Ministerio de Sanidad Servicios Sociales e Igualdad. Diagnosticado un caso secundario de contagio por virus Ébola [press release in Spanish] [Internet]. 2014 [cited 2014 Oct 6]. Available from: http://www.msssi.gob.es/gabinete/notasPrensa.do?id=3427.

49. Ministerio de Sanidad Servicios Sociales e Igualdad. Sanidad y la Comunidad de Madrid constituyen una Comisión de coordinación para realizar el seguimiento del virus Ébola [press release in Spanish] [Internet]. 2014 [cited 2014 Oct 7]. Available from: <u>http://www.msssi.gob.es/gabinete/notasPrensa.do?id=3428</u>.

50. World Health Organization. Ebola response - web portal [Internet]. Geneva: WHO; 2014 [cited 2014 Oct 8]. Available from: https://extranet.who.int/ebola/#/home.

51. Briand S, Bertherat E, Cox P, Formenty P, Kieny MP, Myhre JK, et al. The international Ebola emergency. N Engl J Med. 2014 Sep 25;371(13):1180-3.

52. Frieden TR, Damon I, Bell BP, Kenyon T, Nichol S. Ebola 2014 - new challenges, new global response and responsibility. N Engl J Med. 2014 Sep 25;371(13):1177-80.

53. World Health Organization. Interim infection prevention and control guidance for care of patients with suspected or confirmed Filovirus haemorrhagic fever in health-care settings, with focus on Ebola [Internet]. Geneva: WHO; 2014 [cited 2014 Sep 24]. Available from:

http://apps.who.int/iris/bitstream/10665/130596/1/WHO HIS SDS 2014.4 eng.pdf?ua=1&ua=1.

54. European Commission Humanitarian Aid and Civil Protection. Ebola in West Africa - factsheet [Internet]. ECHO; 2014 [updated 2014 Oct; cited 2014 Oct 8]. Available from:

http://ec.europa.eu/echo/files/aid/countries/factsheets/thematic/wa ebola en.pdf.

55. European Centre for Disease Prevention and Control. Risk assessment guidelines for diseases transmitted on aircraft. Second edition. [Internet]. Stockholm: ECDC; 2010 [cited 2014 Oct 8]. Available from: http://ecdc.europa.eu/en/publications/publications/1012 gui ragida 2.pdf.

56. World Health Organization. International health regulations (2005). Second edition [Internet]. Geneva: WHO; 2008. Available from: <u>http://whqlibdoc.who.int/publications/2008/9789241580410_eng.pdf?ua=1</u>.

57. World Health Organization. Guidance on regulations for the transport of infectious substances 2013–2014 [Internet]. Geneva: WHO; 2012. Available from:

http://apps.who.int/iris/bitstream/10665/780[575/1/WHO_HSE_GCR_2012.12_eng.pdf.

58. European Commission. Commission Directive 2004/33/EC of 22 March 2004 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards certain technical requirements for blood and blood components [Internet]. 2004 [cited 2014 Sep 30]. Available from: <u>http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32004L0033&from=EN</u>.

59. European Centre for Disease Prevention and Control. Risk of transmission of Ebola virus via donated blood and other substances of human origin in the EU. 6 October 2014. [Internet]. Stockholm: ECDC; 2014. Available

from: <u>http://ecdc.europa.eu/en/publications/Publications/ebola-risk-transmission-via-donated-blood-substances-human-origin-october-2014.pdf</u>.

60. European Centre for Disease Prevention and Control. Algorithm for initial assessment and management of patients for Ebola virus disease [Internet]. Stockholm: ECDC; 2014 [cited 2014 Oct 8]. Available from:

http://ecdc.europa.eu/en/healthtopics/ebola_marburg_fevers/algorithm-evd-case-assessment/Pages/default.aspx. 61. European Centre for Disease Prevention and Control. Algorithm for laboratory diagnosis of Ebola virus disease [Internet]. Stockholm: ECDC; 2014 [cited 2014 Oct 8]. Available from:

http://ecdc.europa.eu/en/healthtopics/ebola marburg fevers/algorithm-evd-diagnosis/Pages/default.aspx.

62. World Health Organization. 2014 Ebola Virus Disease (EVD) outbreak in West Africa - Travel and transport risk assessment: Recommendations for public health authorities and transport sector [Internet]. Geneva: WHO; 2014 [cited 2014 29 July 2014]. Available from: <u>http://www.who.int/ith/updates/20140421/en/</u>.

63. World Health Organization. WHO statement on travel and transport in relation to Ebola virus disease (EVD) outbreak. 18 August 2014 [Internet]. Geneva: WHO; 2014 [cited 2014 Oct 8]. Available from: http://www.who.int/mediacentre/news/statements/2014/ebola-travel-trasport/en/.

64. European Centre for Disease Prevention and Control. Infection prevention and control measures for Ebola virus disease - Entry and exit screening measures. [Internet]. Stockholm: ECDC; 2014 Oct 12.

65. European Centre for Disease Prevention and Control. Assessment and planning for medical evacuation by air to the EU of patients with Ebola virus disease and people exposed to Ebola virus. 19 September 2014 [Internet]. Stockholm: ECDC; 2014. Available from: <u>http://www.ecdc.europa.eu/en/publications/Publications/air-transport-EVD.pdf</u>.

66. European Centre for Disease Prevention and Control. Ebola virus disease case definition for reporting in EU [Internet]. Stockholm: ECDC; 2014 [cited 2014 Oct 15]. Available from:

http://ecdc.europa.eu/en/healthtopics/ebola_marburg_fevers/EVDcasedefinition/Pages/default.aspx.