THREAT ASSESSMENT BRIEF

Implications of the Marburg virus disease outbreak in Rwanda for the EU/EEA, 2024

10 October 2024

Summary

This threat assessment addresses the implications of the ongoing Marburg virus disease (MVD) outbreak in Rwanda for the European Union/European Economic Area (EU/EEA). MVD is a severe disease in humans and, although uncommon, it has the potential to cause epidemics with significant case fatality. All recorded MVD outbreaks to date have originated in Africa. MVD is not an airborne disease and is considered not to be contagious before symptoms appear. Direct contact with the blood and other body fluids of infected people and animals or indirect contact with contaminated surfaces and materials like clothing, bedding and medical equipment is required for transmission. The risk of infection is minimised when proper infection prevention and control precautions are strictly followed. There is no approved treatment or vaccine for MVD; however, several pharmaceuticals and candidate MVD vaccines are under investigation.

Epidemiological situation

On 27 September 2024, Rwanda reported its first MVD outbreak. As of 9 October 2024, 58 cases, including 13 deaths, have been reported in the country. According to limited available information, the majority are healthcare workers. Cases have been reported from eight of Rwanda's 30 districts. In response to this outbreak, the Rwandan Ministry of Health is implementing measures such as restrictions on hospital visits and attendance at funerals, measures for educational settings, places of worship, and meetings, as well as a travel advice. Routine temperature checks are conducted at points of entry and exit screening is being implemented at Kigali airport. Vaccination of healthcare workers with an investigative vaccine is also being implemented as part of a study.

Risk assessment

We assess the overall risk for EU/EEA citizens visiting or living in Rwanda as low. This is because the likelihood of exposure to MVD – considering the low number of cases reported and the mode of transmission – and the impact are both assessed as low[1].

In the event of MVD cases being imported into the EU/EEA, we consider the likelihood of further transmission to be very low, and the associated impact low. Therefore, the overall risk for the EU/EEA is assessed as low.

Recommendations

Early detection and rapid isolation of an imported case of MVD, timely contact tracing, and strict infection prevention and control (IPC) protocols are crucial to mitigate further transmission of the virus.

EU/EEA countries should raise healthcare workers' awareness of MVD and the ongoing outbreak for early recognition of people suspected of being infected, and also ensure availability of diagnostics, review viral

[1] Please note that according to the ECDC risk assessment methodology, the impact is assessed at the population level. In this case it is assessed as low since the expected number of MVD cases in EU/EEA citizens in Rwanda is expected to be very small.

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haemorrhagic fever (VHF) case management protocols, make sure healthcare workers are trained in the relevant IPC protocols, and have appropriate PPE available.

Suspected cases (people with clinical manifestations compatible with MVD and with epidemiological links to MVD cases) should be tested. People suspected or confirmed as having MVD should immediately be reported to the EU's Early Warning and Response System as a serious cross-border threat to health alert.

All contacts should be traced and followed up closely for 21 days after the last known contact. High-risk contacts need to be quarantined and may need to be hospitalised for close monitoring.

Risk communication should be undertaken by public health authorities targeting those travelling to and returning from Rwanda. Travellers should be made aware of the ongoing outbreak in the country and be advised to follow all the recommendations of the local health authorities. Specific information should be provided on the symptoms and transmission modes of MVD. Upon return, travellers should be advised how and where to seek medical care if they develop MVD-compatible symptoms, and mention their travel and/or contact history.

Scope and audience

This Threat Assessment Brief is aimed at public health authorities and healthcare experts in the EU/EEA. More information about MVD is available on ECDC's website here.

Epidemiological situation

Marburg virus disease (MVD), formerly known as Marburg haemorrhagic fever, is a severe disease in humans caused by *Marburg marburgvirus* (MARV). Although MVD is uncommon, MARV has the potential to cause epidemics with significant case fatality. All recorded MVD outbreaks have originated in Africa. MVD is not an airborne disease and is considered not to be contagious before symptoms appear. Direct contact with the blood and other body fluids of infected people and animals or indirect contact with contaminated surfaces and materials like clothing, bedding and medical equipment is required for MARV transmission. For more information on the symptoms and clinical picture of MVD please refer to ECDC's 'Factsheet for health professionals about Marburg virus disease' [1].

On 27 September 2024, Rwanda reported that a number of MVD cases had been reported in the country [2]. The first confirmed cases were detected when patients in teaching hospitals were not responding to treatment and they were further tested [3]. The first cases detected were linked to the presumed index case who died in early September 2024 [3,4]. As of 9 October 2024, 58 cases, including 13 deaths and 12 recoveries, have been reported [5].

Based on limited information available for 36 cases reported as of 2 October 2024, they had been reported from eight of Rwanda's 30 districts. The majority of cases were in healthcare workers (80%) and belong to the same cluster in linked healthcare facilities in Kigali [4,6].

On 5 October 2024, the Sabin Vaccine Institute provided 700 doses of the investigational vaccine against Marburg virus (MARV) to Rwanda [7]. The candidate vaccine is based on replication deficient chimpanzee adenovirus type 3 (cAd3), expressing MARV surface glycoprotein (GP) [8]. On 6 October 2024, vaccinations for healthcare workers in Kigali started as part of a Phase 2 rapid response open-label study [7,9].

In response to the outbreak the national authorities of Rwanda have published and are implementing a series of measures such as: increasing awareness on personal hygiene measures; guidelines to avoid contact with symptomatic individuals; ban of visits to hospitals; strengthening implementation of IPC measures around the country; measures to limit contact with dead bodies (no home vigils or open-casket viewings, limiting funeral attendees to 50 persons) [10,11]. Additionally, routine temperature checks are conducted at points of entry and exit screening is implemented at Kigali airport including a health questionnaire and health check with temperature check [12].

ECDC risk assessment for the EU/EEA

This threat assessment is based on data available at the time of publication and follows ECDC's rapid risk assessment methodology, where the overall risk is determined by a combination of the likelihood of infection and its impact [13], with a focus on potential human-to-human transmission. The risk assessment overview is presented in Table 1.

What is the risk associated with the ongoing MVD outbreak in Rwanda for EU/EEA citizens visiting or living in the country?

EU/EEA citizens visiting or living in Rwanda are considered at a low likelihood of exposure and infection, since person-to-person transmission of MARV requires contact with body secretions from a symptomatic person and case numbers remain low. There are still many unknowns around the epidemiological links of those with the disease and the degree of ongoing community transmission of the virus. Control measures announced by Rwanda's government in various settings (educational, places of worship, meetings, funerals) will further mitigate this likelihood.

Transmission of the virus is documented, and most likely ongoing, in healthcare facilities in Kigali, with many healthcare workers affected. Small numbers of EU/EEA citizens may be working in healthcare settings in Rwanda and for them the risk is estimated as higher, particularly if not using proper personal protective equipment (PPE). Healthcare workers, along with caregivers, are at the highest risk of contracting the disease in these outbreaks, due to having close contact with body fluids and performance of invasive procedures [14]. However, information available from the Rwandan Ministry of Health is that they are implementing strict IPC protocols in hospitals around the country and a no-visitor policy for inpatients, which should decrease the likelihood of exposure.

The impact of an MVD case for an EU/EEA citizen in Rwanda is assessed as low. Although MVD is a potentially life-threatening disease, at the population level case numbers are low and in the context of this outbreak adequate supportive care is available locally.

Therefore, the overall risk for EU/EEA citizens visiting or living in Rwanda is estimated as low.

What is the risk for EU/EEA citizens from any imported cases related to the ongoing MVD outbreak in Rwanda?

In the event that MVD cases are imported into the EU/EEA, we consider the likelihood of further transmission to be very low if appropriate measures are taken (e.g. early detection, isolation of suspected cases (i.e. any person with MVD-compatible symptoms and an epidemiological link to the ongoing outbreak in Rwanda) and contact tracing). In addition, the Rwandan Ministry of Health has implemented measures to mitigate the risk of people with MVD leaving the country. Identified contacts of people with MVD in the ongoing outbreak cannot leave the country and in addition, exit screening is being implemented, including health checks, a health declaration and temperature checks [12].

The impact associated with imported MVD cases in the EU/EEA is estimated as low. Hence, the overall risk for EU/EEA citizens from a potential imported MVD case is assessed as low.

Table 1. Overview of risk assessment associated with the MVD outbreak for the EU/EEA

Risk questions	Likelihood	Impact	Overall risk
What is the risk for EU/EEA citizens visiting or living in Rwanda?	Low	Low	**Low**
What is the risk to EU/EEA citizens associated with imported MVD cases connected to the ongoing outbreak?	Very low	Low	**Low**

The assessment above has moderate uncertainty due to the limitations (see section below) of the available epidemiological information.

ECDC recommendations

EU/EEA countries should focus on raising awareness of health professionals about MVD and ensuring availability of diagnostics. In addition, revision of and training on VHF case management protocols including IPC procedures is needed. Availability of PPE should also be ensured. Rapid isolation of cases, timely contact tracing and close monitoring of those at risk are crucial to prevent further transmission in connection to any potential MVD imported case [15,16].

Surveillance, testing and diagnosis of MVD

MVD in humans is notifiable at the EU/EEA level as viral haemorrhagic fever [17]. Please see Annex 1 for a proposed new EU case definition specific for filovirus infections. Suspected cases (i.e. cases with clinical manifestations compatible with MVD and with epidemiological link to MVD cases) should be tested. Cases suspected or confirmed should be immediately reported as a serious cross border threat to health alert using the Early Warning and Response System, which interlinks with EpiPulse to allow the timely assessment of the situation.

Many of the signs and symptoms of MVD are comparable to those of other infectious diseases such as malaria, typhoid fever, dengue, and other viral haemorrhagic fevers (e.g. Lassa fever and Ebola virus disease). Therefore, the confirmation of MVD requires laboratory diagnosis. Molecular methods (e.g, RT-PCR) have been shown to be sensitive, specific, and effective, and are the ones currently most in use. Early diagnosis of suspected cases should be performed by RT-PCR upon onset of symptoms. As a negative result on an early sample does not rule out infection, repeated testing of suspected cases is necessary until recovery.

Other assays (e.g. antigen-capture ELISA, virus isolation, histological techniques and immunohistochemistry) are also available to detect MARV in samples. Serological methods for MVD include ELISA and indirect immunofluorescence assay (IFA). Detection of IgM antibodies against MARV indicates recent infection; such antibodies can be detected as early as two to four days after symptom onset. IgG antibodies can be detected eight to 10 days after symptom onset and persist for up to two years after infection. Only a few commercial diagnostic tests with CE label are available for MVD. The laboratory capability of EVD-LabNet network members is available at: EVD-LabNet directory.

Specimens from MVD patients should be handled in Biosafety Level 3 (e.g. RT-PCR and ELISA on non-inactivated samples) or Level 4 laboratories (virus isolation) under strict biological containment circumstances. RT-PCR and ELISA testing of inactivated samples can be performed at BSL-2 laboratory facilities. Depending on the time course of the infection, the optimal diagnostic procedures for MVD are different. The interpretation of tests results should consider the limitations of the assays. In some cases, it might be necessary to perform repeated tests or additional assays [1]. Based on the laboratory tests' results, cases can be classified as confirmed or as probable or can be discarded.

Treatment

There is no approved, specific antiviral treatment for MVD available. Supportive therapy (intravenous fluids, electrolyte replacement, supplemental oxygen, blood and blood products replacement) may improve the clinical outcome significantly [18], while several antiviral compounds are under investigation [1]. A monoclonal antibody (MBP-091) and the antiviral remdesivir have shown promising results in animals and may be part of clinical trials in the ongoing outbreak in Rwanda [19].

Management of people suspected or confirmed with MVD and infection prevention and control

People suspected or confirmed as having the disease should be isolated, preferably in a negative pressure isolation room or, if not available, a single patient room with a toilet, anteroom, and closing door [15].

The number of healthcare workers caring for the patient should be limited, and they should be trained in the use of the appropriate PPE, which includes water-resistant gown with the potential addition of a plastic apron, boot or shoe covers, two pairs of gloves (latex or nitrile according to EN ISO 374-1:2016), a well fitted FFP2 respirator, and face shield or goggles. Aerosol-generating procedures should be avoided unless PPE and negative pressure room are available. The use of needles and other sharp objects should be avoided as much as possible. Prior to disposal, any item in the isolation ward, including human excreta, must be disinfected with a bleach solution at a concentration of 1:10 [20]. Barrier nursing procedures avoiding contact with blood or body fluids, are the most important infection prevention and control protocols for MVD [21,22].

All staff working in the isolation area, laundering potentially infected linens, disinfecting items or houses, transporting patients, or providing safe burials must wear personal protective equipment [20]. Any contact with the patient's body or fomites should be avoided during the burial process. Decontamination of the body using a 1:10 bleach solution and placement in a body bag are standard burial procedures. The body bag is then closed and the outside of the bag is similarly decontaminated [20].

Due to the persistence of MARV in semen, male recovered patients are advised to practice safe sex with consistent use of condoms for at least 12 months after clinical recovery unless their semen has tested negative on two different occasions [23].

Contact tracing and management of contacts

For the purpose of contact tracing in connection with people with MVD, contacts can be classified as shown in Table 2. All contacts should be traced and followed up closely for 21 days after the last known contact. They should be provided with tailored information to understand the clinical and epidemiological aspects of the disease, as well as instructions on the specific symptoms to look out for, advice to self-isolate in case symptoms develop and contact information with instructions how to seek medical care.

In the case of MVD, contacts are considered not infectious until they develop symptoms, particularly fever. High risk contacts of an MVD case should be followed up daily by public health authorities for 21 days after their last known exposure. Depending on the availability of resources and the adherence of the contact to guidance, contacts can either be hospitalised for monitoring or given specific instructions for strict self-quarantine in a safe place. Daily monitoring can also be performed online. High-risk contacts should not be allowed to travel or work until the 21-day monitoring period is over; teleworking is of course possible. Testing should only be performed if MVD-compatible symptoms develop.

For low-risk contacts, self-quarantine can be used and follow-up by public health authorities can be every other day. If the contact is working in the healthcare sector, they should be excluded from coming into work until the 21-day monitoring period is over. Otherwise, teleworking can be encouraged where possible. Social contacts should be limited to the minimum and travel should be discouraged.

Table 2. Summary of management approach for contacts of a person with MVD

Type of contact	Description	Management
High risk	• Healthcare workers and other auxiliary hospital personnel caring for an MVD patient not wearing PPE or with inadequate PPE • Healthcare workers with PPE reporting a breach in their equipment or suffering a sharps injury or splash exposure (with or without PPE) • Laboratory staff handling specimens and suffering occupational exposure (e.g. sharp or splash exposures) with or without PPE • Care-takers of a person with MVD • Household members • Sexual partners • People cleaning and preparing for burial the dead body of an infected person without appropriate PPE • Any person reporting contact with body fluids of a person with MVD in any other situation	• Monitoring daily by PH authorities for the development of MVD symptoms for 21 days after the last known exposure • Hospitalisation for monitoring or practice strict self-quarantine depending on the PH capacity to monitor and the adherence to guidance • No travelling or working is advised, unless teleworking is possible.
Low risk	• Contact in the asymptomatic phase with a person with MVD with no reported contact with body fluids (e.g. brief social interactions in public, work colleagues or social encounters/ acquaintances) • Healthcare worker contact wearing appropriate PPE	• Self-monitor for possible MVD-compatible symptoms (e.g. fever, vomiting, diarrhoea, back pain, rash) for 21 days after the last known exposure. • Depending on available resources, public health authorities should be in frequent contact with this type of contacts as well (e.g. every other day). • Provide information and instructions to self-isolate in case symptoms develop and how/where to seek medical care. • If the low-risk contact is a healthcare worker, they should be excluded from work until the 21-day monitoring period is over.

Substances of human origin

The presence of MARV in blood and transmission through direct contact with body fluids (e.g. urine, saliva, faeces, vomit, breast milk, amniotic fluid, and semen) suggests that transmission via substances of human origin (SoHO) is possible. However, no cases of transmission of MARV through SoHO have been reported to date. Based on non-human primate models, viraemia is expected to coincide with the appearance of symptoms [24]. However, viral replication occurs in organs such as the liver and spleen [25] and might not be detected through blood tests alone. Rare, mild MARV infections with unspecific symptoms have been reported in previous outbreaks [26]. It is important to note that no donor screening tests exist for MARV.

Prospective donors returning from Rwanda and who are not deferred due to other risks should be interviewed regarding contacts with people with confirmed or suspected MARV infections or, in the context of the current

outbreak, regarding visits or stays in healthcare facilities in the country. It is recommended to defer such donors at risk for exposure for eight weeks (twice the maximum incubation period) since returning from Rwanda. Individuals monitored in the context of public health control measures due to history of contact with people with confirmed or suspected MARV infections or other exposure to MARV should be excluded from donating SoHO for eight weeks from the beginning of the monitoring period.

Risk communication

Member States should increase awareness about MVD among healthcare providers working or preparing to work in Rwanda, including information on clinical presentations and personal protection measures. This should include what symptoms to monitor for, the types of high-risk contact, how and where to seek medical advice and care if they are exposed.

Public health authorities should also increase awareness of MVD among healthcare providers in the EU/EEA. Healthcare workers need to be informed about the clinical presentation of MVD and reminded to explore travel history in connection to symptoms in their patients. They should be given information how to protect themselves in the event of discovery of a suspected case, as well as where to get advice, where testing is available and how it can be requested.

Risk communication in connection to a potential imported case should be prompt and transparent, explaining the risks from the disease as well as the response measures. Frequent updates should be provided about potential cases and testing results. Tailored information and guidance should be provided to contacts under monitoring.

Travel advice and information to travellers

Information about the health risks related to the ongoing MVD outbreak should be provided to EU/EEA travellers going to Rwanda as well as EU/EEA citizens working or living in Rwanda. They should be made aware of the ongoing outbreak in the country and the affected areas and advised to follow the recommendations of the local health authorities, as regards hospital visitation, attending education settings, places of worship and meetings and funerals [2,10-12].

They should be advised to:

- Avoid contact with persons exhibiting MVD symptoms (like fever, vomiting, diarrhoea or bleeding) or contact with fomites contaminated by body fluids of infected persons. This includes avoiding participating in funerary rituals and the burial process of deceased persons.
- Avoid visiting healthcare facilities in the MVD-affected areas for non-urgent medical care or for non-medical reasons.
- Avoid habitats that may be populated by bats, such as caves or mines, as well as any form of close contact with wild animals, including monkeys, forest antelopes, rodents, and bats, both alive and dead, and manipulation or consumption of any type of bushmeat.

Travellers returning from Rwanda to the EU/EEA should be advised to seek prompt medical care if they develop MVD-compatible symptoms and mention their travel history, as well as possible exposure history and close contacts.

Please see Annex 2 for travel advice jointly developed by ECDC and World Health Organization (WHO) Regional Office for Europe experts.

As regards travel measures, no travel restrictions are currently recommended in the context of this outbreak for EU/EEA citizens travelling to Rwanda. The Rwandan government has implemented exit screening at Kigali airport, including a health questionnaire, health and temperature checks, as per WHO guidance [27]. Currently available limited scientific evidence based on the experience from the Ebola outbreak 2014–2016, supports exit screening from an area or country affected by viral haemorrhagic fever outbreak rather than entry screening, as a measure to prevent the introduction of cases to other countries, if implemented properly [28].

Limitations

This assessment is based on outbreak information made available by the Ministry of Health of Rwanda as of 9 October 2024. Daily updates are published on the number of tests performed, cases, and deaths. The Ministry of Health reported on 9 October 2024 that all new cases are part of the same cluster linked to healthcare facilities in Kigali. However, more detailed data on case characteristics, including dates of symptom onset and/or diagnosis, demographics, and the epidemiological links and chains of transmission, have not been well documented in epidemiological reports.

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Annex 1. Proposed case definition for EU/EEA level surveillance of filovirus infections

Clinical criteria

- Clinical manifestations compatible with filovirus infection (e.g. fever, gastrointestinal symptoms, haemorrhagic manifestations, central nervous system manifestations)

Laboratory criteria

A. Probable case

- Detection of acute infection through serological methods (e.g. IgM antibodies in a single serum sample, seroconversion or four-fold antibody titre increase in paired serum samples, low avidity IgG antibodies in a serum sample).

B. Confirmed case

At least one of the following three:

- Isolation and identification of filovirus from a clinical specimen;
- Detection of filovirus nucleic acid from a clinical specimen;
- Detection of filovirus antigen from a clinical specimen.

Identification of the virus species should be performed, if possible.

Epidemiological criteria

At least one of the following two:

- Having been exposed within the four-week period prior to the onset of symptoms to a case of filovirus infection;
- Having been exposed to filovirus infectious material during an occupation (e.g. laboratory work).

Case classification

A. Possible case

NA

B. Probable case

Any person meeting the laboratory criteria for a probable case AND at least one of the following two:

- clinical criteria
- epidemiological criteria

C. Confirmed case

Any person meeting the laboratory criteria for a confirmed case.

Annex 2. Public health advice for people travelling to or from countries with outbreaks of Marburg Virus Disease

(Developed jointly with WHO Regional Office for Europe)

An MVD outbreak is currently ongoing in Rwanda. If you are travelling to or returning from Rwanda:

- Avoid contact with anyone who shows MVD symptoms (like fever, vomiting, diarrhoea or bleeding) or with materials and surfaces contaminated by their body fluids. Keep your distance from infected individuals, including dead bodies. Avoid participating in funerary rituals.
- Avoid visiting healthcare facilities in the MVD-affected areas, unless it's an emergency.
- Avoid places where bats may live, such as caves or mines. Avoid close contact with wild animals, including monkeys, forest antelopes, rodents, and bats, both alive and dead. Do not touch or eat any type of bushmeat.

Have you recently come back from Rwanda?

If you've returned from Rwanda within the previous 21 days and experience symptoms like high fever, severe headache, muscle pain, isolate yourself and contact a doctor right away. Tell them about your trip, any risky situations you were in, and people you were close to.

What you need to know about Marburg

Transmission

Marburg virus disease (MVD) is a severe disease that typically spreads through direct contact with blood or other body fluids from infected people or animals.

The virus can also be transmitted through contact with surfaces and materials like clothing, bedding and medical equipment contaminated with infected blood or body fluids.

If proper protective measures are strictly followed, the likelihood of infection is very low.

Symptoms

Early symptoms of MVD appear two to 21 days after infection and may include high fever, chills, severe headache and severe tiredness, muscle aches and pains.

As infection progresses, patients may experience nausea, vomiting, stomach and or chest pain, rash and diarrhoea which can last around a week. In later stages of the disease, bleeding from various sites such as the gums, nose and anus can occur. Patients can suffer shock, delirium and organ failure.

Early care for MVD can significantly improve chances of survival and reduce the risk of transmission to others.

Information
Get information, advice and guidance on MVD from official sources of information, such as your national and local health authority and WHO. Always check the source and analyse the content before sharing it with others.