RAPID RISK ASSESSMENT

Rift Valley fever outbreak in Mayotte, France

7 March 2019

Main conclusions and options for response

Between the end of November 2018–1 March 2019, regional authorities reported 82 human Rift Valley fever (RVF) cases across Mayotte. These cases are concentrated mainly in the Centre-West and North of the island, affecting mainly rural areas. No fatalities have been reported to date.

Travellers to and residents of Mayotte are at very low risk of infection if they apply appropriate preventive measures. However, those who are in contact with potentially infected animals (e.g. veterinarians and those involved in livestock farming, butchering and slaughtering of animals in RVF-affected areas) have an increased risk of infection with RVF virus (RVFV) and should therefore handle potentially infected animals in a secure manner by practising safe animal husbandry and slaughtering practices. In affected areas, consumption of raw milk and eating animal products that have not been thoroughly cooked should be avoided. In addition, as a precautionary measure, personal protective measures against mosquito bites should be applied. Transmission of the virus through contact with blood or infected materials in healthcare settings can be prevented by applying the measures defined in WHO's 'Standard precautions in health care' aide-memoire.

The occurrence of travel-related cases returning to the continental EU/EEA is not new as RVF is endemic in many African countries. Indeed, sporadic importation of human RVF cases into the EU/EEA has occurred in the past. Importation of RVF human cases from Mayotte to the EU/EEA cannot be excluded, particularly to connected EU Outermost Regions in the Indian Ocean (Réunion). Accordingly, EU Member States should maintain awareness of the epidemiological situation of RVF in Africa, including in the Outermost Regions in the Indian Ocean, and the countries of the Arabian Peninsula and continue to include RVF in their differential diagnosis for sick returning travellers. Should the virus be imported through a human case, the likelihood of further sustained transmission to humans is very low, as direct human-to-human sustained transmission has not been described for RVF. As a precautionary measure to reduce the risk of potential vector-borne transmission between humans, imported viraemic RVF cases should be advised to apply personal protective measures against mosquito bites in areas with competent and active vectors.

Overall, the current outbreak in Mayotte probably poses a very low risk for EU/EEA countries in terms of introduction of RVF through the animal trade as imports into the continental part of the EU of live animals and their meat and milk from Mayotte are probably very rare, due to the distance. Should the virus be introduced into continental EU/EEA countries through imported infected animals from an RVF area in Africa, the likelihood of further vector-borne transmission among animals remains very low during the winter season due to the low-level abundance and activity of competent mosquito vector populations in continental EU/EEA countries, although it cannot be excluded. Similarly, another risk that cannot be excluded could be the illegal transport of fresh meat and unpasteurised milk and untreated products from infected ruminants in personal luggage.

The risk of transmission through infected substances of human origin (SoHO) is very low. ECDC will monitor the situation in Mayotte and update its assessment should the risk for the EU change.

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Public health issue

This rapid risk assessment (RRA) addresses the risk of importation of Rift Valley fever (RVF) virus (RVFV) and further spread of the virus within the European Union/European Economic Area (EU/EEA) in relation to the recent increase in cases reported on Mayotte, France.

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Disease background information

Rift Valley fever (RVF) is an acute febrile zoonotic disease that primarily affects animals, but can also cause illness in humans. It is a well known disease in livestock in Africa associated with epizootic events with high mortality and abortion rates in domestic ruminants. The pathogenesis of the disease varies depending on the animal species and age. Newborn lambs, kids and calves frequently develop an acute form of the disease with high mortality (up to 100%) compared to older animals. More information is available in EFSA's story map on RVF [1].

The disease is caused by *Rift Valley fever phlebovirus* species, genus *Phlebovirus*, family *Phenuiviridae* [2]. RVFV was first isolated in 1931 during an epidemic among sheep in the Rift Valley in Kenya [3]. RVFV circulation in most African countries and certain Middle Eastern countries has been documented by serological surveys, animal and human cases and outbreak reports [4–7]. Since 2000, epizootic events associated with human cases have been reported in Saudi Arabia and Yemen (2000–2001), Egypt (2003), Kenya, Tanzania and Somalia (2006–2007); Sudan (2006-2007); Madagascar (2008–2009), South Africa and Namibia (2009–2011); Mauritania (2010, 2012–2015); Senegal (2013–2014); Uganda (2016); Niger (2016); Kenya (2018) and South Sudan (2018) [8-14].

In Mayotte, human infections were detected for the first time in 2007–2008 [15]. Since 2008, every patient presenting with a dengue-like syndrome undergoes systematic laboratory investigation for dengue fever, chikungunya virus disease, RVF and leptospirosis [16]. From July 2007–July 2009, 13 laboratory-confirmed RVF cases were reported [17]. Further molecular analysis demonstrated that RVFV was genetically closely linked to the 2006–2007 isolates from Kenya [18]. Prior to the current outbreak, no human cases had been reported in Mayotte since 2013 [16].

RVFV circulation among livestock in Mayotte has been retrospectively identified since 2004 based on serosurveys [19]. A serosurvey based on cattle serum collected from June 2007–May 2008 in Mayotte showed a RVF island-wide seroprevalence of 10.6% (95% CI 7%–14%) [19]. Annual prevalence (IgG and IgM) in animals was observed to have increased to 36% in 2008–2009 (95% CI 17%–55%) [20]. Subsequently, a continuous decrease in annual seroprevalence of IgG against RVFV among domestic animals was observed in Mayotte from 2009–2015 [20,21].

Transmission

Among animals, RVFV is primarily transmitted by the bite of infected mosquitoes mainly belonging to the *Aedes* and *Culex* genera (but also of *Anopheles* and other mosquito species) [7,22-24]. The virus circulates between animals within an enzootic cycle with long inter-epizootic periods. Vertical transmission also takes place in ruminants [25,26] and vectors [24]. There is limited evidence for direct contact transmission from infected ruminants to healthy [27-29].

The eco-epidemiology of RVF is complex and transmission patterns differ across ecosystems, involving multiple competent mosquito vectors and animal species [22,28,30]. Epizootics can occur when environmental conditions favour vector population growth, such as irrigated and riverine ecosystems and pastoral ecosystems after heavy rainfalls, supporting subsequent virus amplification or when the virus is introduced into naïve animal populations by livestock movements associated with short or long distance trade [6,7,31,32].

In general, spillover to humans occurs concomitantly to epizootic events. The main route of infection of humans is through direct or indirect contact with the blood, body fluids, tissues and organs of infected animals and aborted

animal foetuses. Infection can occur through inoculation (e.g. contact with abraded/broken skin or wound needle-stick injuries) and inhalation of aerosolised infectious body fluids. Consequently, transmission to humans is associated with various occupational and exposure hazards, particularly activities related to slaughtering, skinning or butchering of infected animals and veterinary practices (e.g. assistance during calving/lambing or abortions due to contact with blood or any other infected animal tissue). Dietary exposure (e.g. raw or unpasteurised milk) has been identified as a risk factor for RVFV infection [33,34]. Mosquito bites have been identified as a risk factor for RVF in humans [8,35]. To date, there is no documented direct horizontal human-to-human transmission [8,28], although vertical transmission of RVFV from mothers to their newborn children has been occasionally reported [36,37].

Incubation period and symptoms

The incubation period in humans varies from two to six days [38]. Viraemia is usually seen during the first three days of fever [39]. Approximately 50% of infected humans remain asymptomatic, while the majority of symptomatic cases develop a relatively mild and non-specific flu-like disease with fever lasting around four to seven days. A small percentage of clinical cases may develop more severe medical conditions: haemorrhagic fever associated with a hepatotropic disease (around 1%), delayed neurological disease (around 5% of cases) or ocular complications (around 1%) with haemorrhagic retinal lesions [8,28,40].

Clinical manifestations in animals vary depending on age and animal species [28,41]. After a short incubation period of one to six days, signs may range from mild to severe, including haemorrhagic fever [42]. Abortions are frequent and are often the first indication of development of epizootics in livestock. Mortality is high in newborn and young susceptible animals [43].

At-risk groups

The groups at greatest risk of infection in RVF-affected countries are veterinarians and people involved in livestock farming, butchering and slaughtering. People living or visiting areas where the virus is circulating are at risk of infection through the transmission routes mentioned above [8]. A cross-sectional study among febrile pregnant women in an area endemic for Rift Valley fever in Sudan identified an acute Rift Valley fever virus infection as a significant predictor of having a miscarriage (adjusted odds ratio 7.4, 95%
CI 2.7%–20.1%) [44].

Diagnostics and diagnostic capacity in EU/EEA

The combination of serological and molecular assays is essential to provide laboratory confirmation of RVFV infection.

RVFV can be detected in human blood specimens up to days 4–5 post onset of symptoms by reverse transcription polymerase chain reaction (RT-PCR) and/or virus isolation. Late detection by RT-PCR using the whole blood specimen has been reported and might support enlarging the window for the use of molecular tools for RVF diagnosis [45,46].

Serology is usually by antigen-capture enzyme-linked immunosorbent assay (ELISA). IgM response is measurable from days 5–6 and usually lasts for 2–3 months while IgG typically can be detected from day 8 onwards and persists for several years.

A few commercial diagnostic tests are available for humans and animals. More background on laboratory aspects of RVFV diagnosis can be found in a review by Mansfield and colleagues [47]. A complete overview of RVFV diagnostic capacity in the EU/EEA can be found in the EVD-LabNet directory [48].

Rift Valley fever virus is a Risk Group 3 pathogen according to National Institutes of Health (NIH) guidelines (Appendix B-III-D, Risk Group 3, RG3) and a Group 3 biological agent according to Directive 2000/54/EC of the European Parliament and of the Council [49]. RG3 pathogen and samples from suspected cases should be handled accordingly following appropriate Biosafety Levels (BSL 3) [28,50].

Surveillance in EU

RVF in animals is a notifiable disease in the EU in accordance with Council Directive 82/894/EEC [51] and measures to prevent and control RVF are laid down in Council Directive 92/119/EEC [52]. The importation of live animals from neighbouring countries into the EU is regulated [53]. RVF is also a notifiable disease for the World Organisation for Animal Health [54].

RVF in humans is a notifiable disease at the EU/EEA level under the 'viral haemorrhagic fevers' case definition in accordance with Commission Decision 2018/945/EC. To date, no autochthonous cases or outbreaks of RVF have been reported in continental EU/EEA countries.

From 2012–2017, EU/EEA countries reported seven travel-related RVF cases. Two cases were reported for 2012 by France and the United Kingdom, probably infected in Comoros and Egypt respectively [55]. For 2013, the United Kingdom reported one case, probably infected in Uganda [56]. For 2015, France reported one case, probably infected in Mali. For 2016, France reported three cases, two of which were probably infected in Mali and one in Ghana. For 2014 and 2017, EU/EEA countries did not report any cases of RVF [56].

Prevention and treatment

Control measures to prevent the spread of the virus from animals to humans include sanitary restrictions relating to products of animal origin, such as meat and milk, appropriate disposal of dead animals, information campaigns about at-risk practices (see above) and prevention measures especially targeting risk groups involved in animal husbandry and slaughtering practices (e.g. practicing hand hygiene and use of appropriate individual protective equipment when slaughtering animals or handling sick animals or infectious tissues).

In epizootic areas, all animal products should be thoroughly cooked before consumption and applying personal protective measures against mosquito bites is advisable [8,57]. In healthcare settings, the application of standard infection prevention and control measures described in WHO's aide-memoire 'Standard precautions in health care' are effective for preventing transmission [8,58]. There is no licenced vaccine for humans.

In the EU, any suspicion of disease in animals is subject to restrictions placed on the entire holding until RVF can be ruled out. Confirmation of disease results in culling and destroying the entire herd affected and establishment of a protection and surveillance zone around the holding. Prevention relies on strict import controls. Vaccination is currently prohibited in the EU, but may be authorised under special conditions. Vaccination against RVF has been used to reduce infection in ruminants. Mathematical models developed by Chamchod et al. support the theory that vaccination helps to reduce the severity of RVF outbreaks and quick implementation of vaccination is crucial in reducing the magnitude of the outbreak and endemic number of RVFV [59].

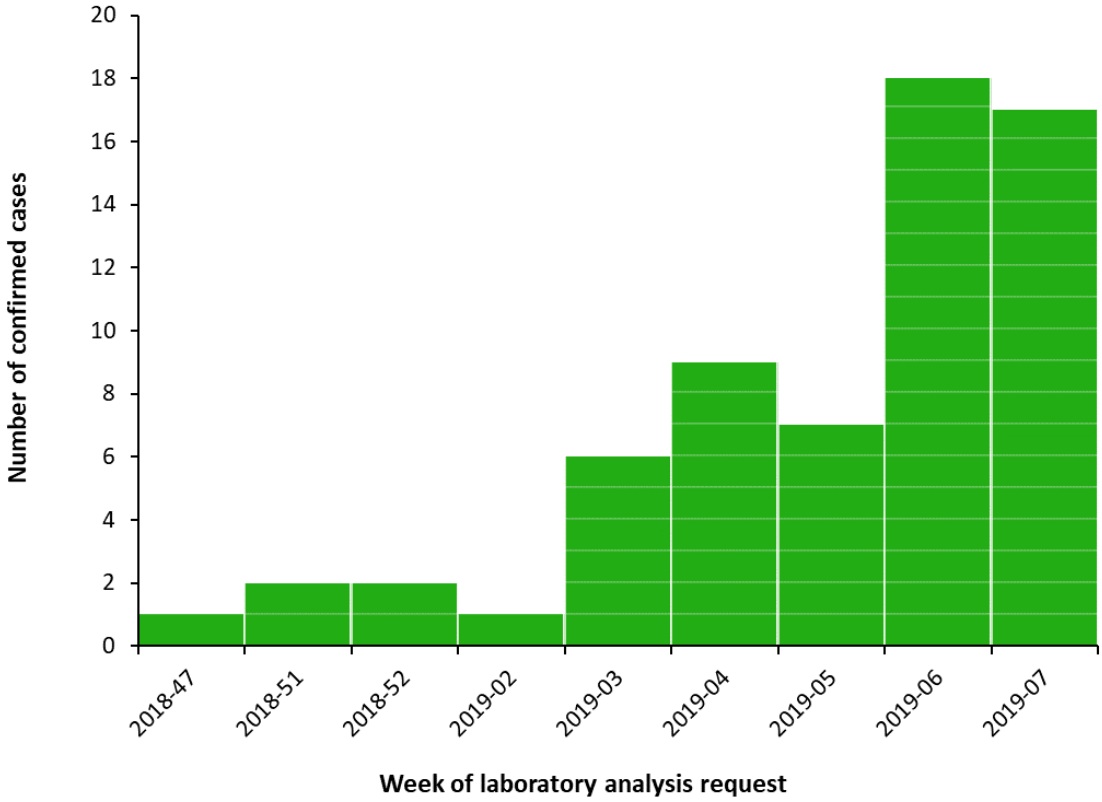
There is no specific treatment for humans or animals.

Event background information

Epidemiological situation of human cases

Between the end of November 2018–1 March 2019, regional authorities reported 82 human RVF cases across Mayotte (Figure 1) [16,60-62]. Among those, 63 were laboratory-confirmed. No fatalities have been reported to date. As of 21 February 2019, the majority of the cases were male (with a male-to-female ratio of 4:1) and a median age of 38 years (age range from 10–74 years) [61]. Since the beginning of the outbreak, 36 cases have been investigated: 26 cases are reported to have had direct or indirect contact with animals, 15 cases had consumed raw or curdled milk, while five cases were unaware of any direct or indirect contact with livestock [61].

Figure 1. Distribution of confirmed human cases of RVF in Mayotte (n=63) by week of laboratory analysis request, 22 November 2018–21 February 2019

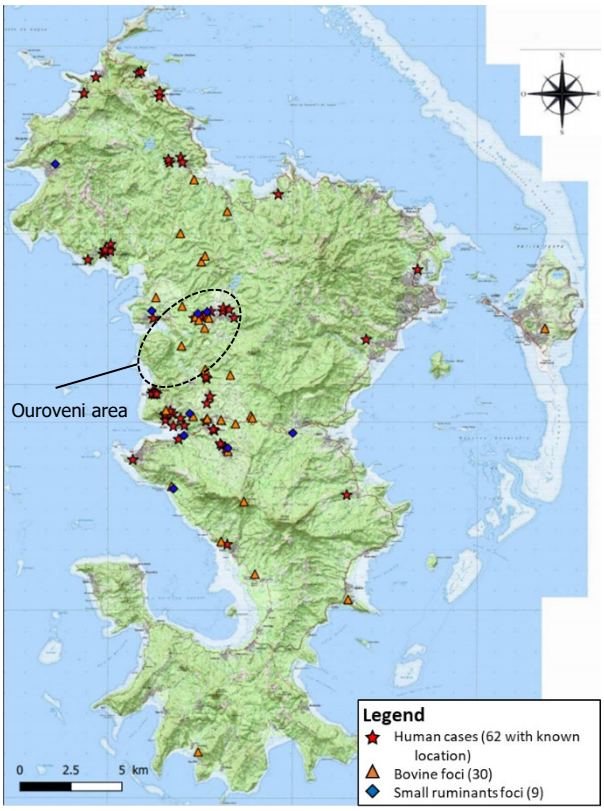


Source: adapted from Agence de Santé Océan Indien Communiqué de presse 1 mars 2019 [62].

Human cases are concentrated mainly in the Centre-West and North of Mayotte (Figure 2). Commune of residence is available for 34 of the confirmed cases as follows: Chiconi (n=10), Tsingoni (n=6), M'tsangamouji (n=6), Bandraboua (n=5), Ouangani (n=4), Mtsamboro (n=2) and Sada (n=1) [61]. The investigations of 36 confirmed human cases showed a possible direct or indirect link with the Ourovéni area, which is an agricultural area between the villages of Combani and Kahani with residents owning fields and livestock. This area is well known for hiking activities [61].

Information on environment and type of accommodation was available for 29 cases: confirmed human cases declared living in rural (10 cases), semi-urban (14) and urban areas (5). Results from captures of mosquitoes in living areas was available for 8 confirmed human cases showing different mosquito species present in the domicile with a predominance of *Culex* spp. [61].

Figure 2. Geographic distribution of human cases (stars), animal outbreaks in cattle (triangles) and small ruminants (diamonds) of RVF in Mayotte, 22 November 2018–1 March 2019



Source: adapted from Agence de Santé Océan Indien Communiqué de presse 1 mars 2019 [62].

Animal health situation

Samples taken by veterinarians between 22 November 2018–1 March 2019 from sick animals or abortions have identified 39 epizootic foci in Mayotte, each comprising one to six animals, including bovines (30 foci) and small ruminants (9 foci; Figure 2) [62].

According to Mayotte's livestock cooperative, CIRAD and previous published serosurveys, the seroprevalence of RVF among ruminants in Mayotte decreased steadily between 2008–2010 and 2017 [20,21] , then increased in 2017–2018 (3.6%, 95% CI 2.3%–5.6%) and 2018–2019 (10.1%, 95% CI 6.5%–15.3%) [61].

Risk reduction measures

According to local public health authorities in Mayotte, farmers are required to promptly report any sick animals or abortions occurring in their animals to veterinarians in order to take samples for RVF laboratory investigation. To prevent disease, farmers and people who practice slaughtering are invited to wear a mask, gloves and glasses when slaughtering and wash their hands with soap after handling animal or animal tissues. Recommendations have been issued to the population to cook the meat, boil the milk and protect themselves against mosquito bites. In addition, as of 27 February 2019, selling raw milk has been prohibited for a period of three months [63].

ECDC threat assessment for EU/EEA

An epizootic of RVF in Mayotte is an unusual event but not unexpected, as the virus has circulated among animals on several islands of the Indian Ocean, including on Mayotte, since 2004 [64]. Recent serosurveys and animal case reports indicate an increased circulation of RVFV in the livestock of Mayotte at the end of 2018 [20,61]. The sustained viral circulation on Mayotte is possibly due to the continuous presence of susceptible animals, existence of competent vectors maintaining transmission locally and possible regular reintroduction of the virus from nearby countries through illegal domestic animal movements [20,21]. Several mosquito species that have been identified as possible RVF vectors are present on Mayotte [64–66] and current weather conditions are favourable for the vector population (rainy season from December to March). Therefore, further transmission among animals on Mayotte is likely and the associated risk for human infection remains.

Risk for EU/EEA citizens residing in/travelling to affected areas

The occurrence of human cases with known risk behaviour during an epizootic of RVF, such as reported during this outbreak in Mayotte, is consistent with the literature [28,60].

Travellers and residents applying infection prevention measures are at very low risk of infection. Those who are in contact with potentially infected animals, e.g. veterinarians and those involved in livestock farming, butchering and slaughtering of animals in RVF affected areas, however, have an increased risk of infection with RVFV and should therefore handle potentially infected animals in a secure manner by practicing safe animal husbandry and slaughtering practices. In affected areas, consumption of raw milk and of animal products that have not been thoroughly cooked should be avoided. In addition, as a precautionary measure, personal protective measures against mosquito bites should be applied [8,57]. Transmission of the virus through contact with blood or infected material in healthcare settings can be prevented by applying the measures defined in WHO's 'Standard precautions in health care' aide-memoire [58].

Risk of importation to and further spread within EU Outermost Regions in the Indian Ocean

Between 2018–February 2019, there were no official movements of cattle, sheep or goats towards the EU/EEA from the region of the Comoros Islands (Comoros and Mayotte) and Madagascar. Nevertheless, the RVF-free islands of the Indian Ocean Area (Réunion, Mauritius and Seychelles) remain at risk of introduction through illegally imported viraemic animals originating from areas with RVFV circulation, such as countries from eastern Africa and islands of the Indian Ocean (Comoros and Madagascar). As such, early detection of RVF among animals remains a priority in the RVF-free islands of the Indian Ocean Area [14]. Should the virus be introduced, further transmission remains possible due to the presence of naïve livestock and a competent and active mosquito vector population in Réunion [14].

Importation of human cases from Mayotte to Réunion cannot be excluded due to the regular flight connection between the two islands. According to the International Air Transport Association (IATA), there were 67 000 travellers from Mayotte to Réunion in 2017. However, should the virus be imported, the likelihood of further spread by direct human-to-human transmission is very low as sustained direct human-to-human transmission has not been described for RVF. As a precautionary measure, imported viraemic RVF cases should be advised to apply personal protective measures against mosquito bites in areas with competent and active vectors [8,57].

Risk of importation to and further spread within continental parts of EU/EEA

According to EFSA, RVFV can be introduced by illegally imported infected animals and less likely through infected vectors or illegally imported contaminated animal products [22,67]. Imports into continental EU countries of live animals and their meat and milk from Mayotte are probably very rare due to distance, so the risk of introduction of RVF through such trade is probably very low.

Potential RVFV vectors are present in parts of the continental EU/EEA, raising concern about the transmission potential of RVF in Europe [22,68–74]. Overall, further localised transmission between domesticated animals and subsequent RVF cases in humans after virus introduction would require adequate temperatures for vector development and pathogen replication, favourable environmental conditions for sufficient abundance of competent vectors and a large population of susceptible ruminants [24,68]. To date, the likelihood of further spread in continental EU/EEA countries is very low due to both a low probability of importing viraemic animals and the current low winter abundance of competent mosquito vectors, although it cannot be completely excluded.

According to IATA data, there were almost 40 000 travellers from Mayotte to continental Europe in 2017, the vast majority of them to France (97%). Therefore, the importation of human cases from Mayotte cannot be excluded. The occurrence of travel-related cases returning to continental EU/EEA countries is not new as RVF is endemic in many African countries. Sporadic importation of RVF human cases into the EU/EEA has occurred in recent years [46,56]. To date, no autochthonous human cases of RVF have been reported in continental parts of the EU/EEA.

The risk for secondary cases in the EU/EEA through direct human-to-human transmission is negligible, including any secondary transmission from viraemic passengers travelling in airplanes. The probability of further vector-borne transmission within the human population is very low. Transmission of the virus through contact with blood or infected materials in healthcare settings may occur, but can be prevented by applying the measures defined in WHO's 'Standard precautions in health care' aide-memoire [58] and in ECDC's technical report on core competencies for infection control and hospital hygiene professionals in the EU [75].

Rift Valley fever and safety of SoHO

Transmission of RVF through transfusion and/or transplantation has not been reported. Nonetheless, the transmission of RVFV through substances of human origin (SoHO) donated by an asymptomatic viraemic donor cannot be excluded. Since Mayotte is endemic for malaria [76], the deferral period for donors returning from areas affected by malaria is sufficient to prevent the donation of RVF-virus-infectious SoHO. Therefore, the risk of SoHO donation by an RVFV-infected traveller from Mayotte can be considered to be very low. Local blood safety authorities in the Indian Ocean (Établissement Français du Sang, Réunion) ensure the supply of labile blood products from Réunion to the Mayotte hospital depot because there are no blood donations due to the presence of malaria [28].

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