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Rift Valley Fever – epidemiological update and risk of introduction into Europe

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Abstract

Rift Valley fever (RVF) is a vector-borne disease transmitted by a broad spectrum of mosquito species, especially Aedes and Culex genus, to animals (domestic and wild ruminants and camels) and humans. Rift Valley fever is endemic in sub-Saharan Africa and in the Arabian Peninsula, with periodic epidemics characterised by 5–15 years of inter-epizootic periods. In the last two decades, RVF was notified in new African regions (e.g. Sahel), RVF epidemics occurred more frequently and low-level enzootic virus circulation has been demonstrated in livestock in various areas. Recent outbreaks in a French overseas department and some seropositive cases detected in Turkey, Tunisia and Libya raised the attention of the EU for a possible incursion into neighbouring countries. The movement of live animals is the most important pathway for RVF spread from the African endemic areas to North Africa and the Middle East. The movement of infected animals and infected vectors when shipped by flights, containers or road transport is considered as other plausible pathways of introduction into Europe. The overall risk of introduction of RVF into EU through the movement of infected animals is very low in all the EU regions and in all MSs (less than one epidemic every 500 years), given the strict EU animal import policy. The same level of risk of introduction in all the EU regions was estimated also considering the movement of infected vectors, with the highest level for Belgium, Greece, Malta, the Netherlands (one epidemic every 228–700 years), mainly linked to the number of connections by air and sea transports with African RVF infected countries. Although the EU territory does not seem to be directly exposed to an imminent risk of RVFV introduction, the risk of further spread into countries neighbouring the EU and the risks of possible introduction of infected vectors, suggest that EU authorities need to strengthen their surveillance and response capacities, as well as the collaboration with North African and Middle Eastern countries.

Keywords: Rift Valley Fever, introduction, vectors, mosquitoes, livestock, transmission

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Summary

No RVF outbreaks in humans or animals have been reported in Europe or in European Union (EU) neighbouring countries so far, although RVF reappeared after 10 years in a French overseas Department (Mayotte) with outbreaks involving multiple human cases in 2018–2019. Besides this reoccurrence, a legislative process triggered a mandate from the European Commission to European Food Safety Authority (EFSA) to perform a risk assessment on RVF. The Commission adopted a draft Commission Delegated Regulation which supplements Part III of Regulation (EU) 2016/429 (Animal Health Law), laying down rules for the prevention and control of transmissible animal diseases, and that replaces existing Directives, such as Directive 92/119/EEC which currently provides for measures to apply in the event of occurrence of certain diseases, which includes RVF. Additionally, in accordance with Commission Implementing Regulation (EU) 2019/1882, RVF is categorised as a Category A disease.

Following the categorisation and the proposed changes to the measures for RVF, the Commission requested a complete risk assessment on RVF (risk of introduction, exposure and effectiveness of prevention and control measures), since the measures proposed in the Delegated Regulation should be based on the latest scientific knowledge.

In particular, it was requested to provide an update of the global epidemiological situation in relation to RVF with emphasis on areas posing a higher risk for the EU. Moreover, the overall risk of introduction of RVF into the EU (combining rate of entry, RVFV transmission and establishment) should be assessed at regional level (considering the EU regions as specified in a 2017 EFSA scientific opinion on vector-borne diseases) and for each single MS. Regarding the recent epidemics in Mayotte the probability of overwintering of RVF, the risk of RVF spreading from Mayotte to other areas as well as the impact of the disease on animal health and farm production should be assessed. Additionally, the assessment of effectiveness of preventive and control measures in eliminating or reducing the disease impact in Mayotte as well as different surveillance strategies in animals that may be used for detection and possible prediction of RVF recurrence in Mayotte should be carried out. Finally, while considering the risk of RVF introduction into the EU, the surveillance measures for early detection of the disease as well as the feasibility, availability and effectiveness of the prevention and control measures for RVF should be evaluated, especially the ones foreseen in the above-mentioned Commission Delegated Regulation.

The present opinion deals with the update of the global epidemiological situation in relation to RVF with emphasis on areas posing a higher risk for the EU and with an assessment of the overall risk of introduction of RVF into the EU. Two further scientific outputs will be produced to address the other requested points.

For the update on the global epidemiological situation of RVF, descriptive statistics and information from the literature and national authorities were used. Outbreak data from World Organisation for Animal Health (OIE), Animal Disease Notification System (ADNS), WHO, trade data from EUROSTAT and UN COMtrade and information obtained by French authorities and OIE representatives in Middle East were collected and considered.

Rift Valley fever is a vector-borne disease transmitted by a broad spectrum of mosquito species, *Aedes* and *Culex* genus being the most relevant, to animals (domestic and wild ruminants, camels) and humans. RVF has been present historically in Africa in sub-Saharan areas and in specific zones of the Arabian Peninsula, on the border between Saudi Arabia and Yemen. Historically, in these endemic areas, major RVF epidemics have been periodically observed, usually with long inter-epizootic periods (5–15 years) during which the virus was not detected in domestic animal populations.

In the last two decades, some changes in the RVF epidemiology were recorded: more evidence has been observed on the spread of RVFV into new African areas, not regarded as infected before, even in locations considered not optimal for mosquito-borne diseases, like Sahel areas. Moreover, regarding RVF recurrence, epidemics have been recorded more frequently and low-level enzootic RVFV circulation in livestock has been demonstrated in various areas.

Outbreaks in a French overseas department and some seropositive cases detected in Turkey and Tunisia raised concerns for the EU regarding a possible incursion into countries neighbouring continental EU and/or with direct trade links. Positive serological findings in Algeria, Western Sahara, Tunisia, Libya, Iraq, Iran, Turkey, which are or were countries considered officially free from RVF, must be carefully interpreted on the bases of the study designs and diagnostic tests used. However, the repeated detection of serological positive individuals (animals or humans) in these countries must be seen as a signal of a potential risk of RVF spread out of its endemic geographical area.

In this regard, the movement of live animals is the main risk factor for RVF spread from the African endemic areas. Several pathways of livestock movements between sub-Saharan and North African countries can be identified. Moreover, the trade from the Horn of Africa towards the Arabian Peninsula and Middle East involves several millions of live animals each year, thus representing a constant risk of RVF introduction into the Middle East.

Among available diagnostic tools, molecular assays for RVFV detection are available and, more recently, a pen-side test for early detection of viraemic animals. Serological tests to detect RVF antibodies that are able to distinguish early from past RVFV infection in domestic ruminants are also available. As for the EU preparedness, the diagnostic capacity of laboratories among EU Member countries and in the Mediterranean region has been assessed and the level of performance considered adequate as well as in National Laboratories from Algeria, Mauritania, Morocco, Tunisia, Mali and Senegal. Nevertheless, an evaluation of the performance of diagnostic tests in place in most of the other Mediterranean countries should be encouraged through inter-laboratory trials.

Regarding vaccines against RVF, no vaccines have been authorised for use in the EU. However, both live-attenuated and inactivated vaccines are commercially available for RVF and have contributed significantly to the control of RVF in endemic countries. Some limitations are linked to the need of repeated vaccinations for inactivated vaccines, and some safety issues arise for the live-attenuated vaccines. Novel DIVA vaccines, including accompanying DIVA tests, are in the final stages of validation.

The risk of introduction of RVFV into EU was assessed by using a model already presented in an earlier risk assessment by EFSA (2017) for 36 vector-borne diseases. This model is called MINTRISK (Method to INTegrate all relevant RISK aspects) and allows the assessment of the risk of introduction, transmission and impact of vector-borne diseases in a systematic, semi-quantitative way, and can be used for risk evaluation, risk comparison and risk ranking of possible vector-borne diseases of livestock. The risk of introduction of RVF assessed by MINTRISK derives from the combination of the rate of entry (of the pathogen), level of transmission (as the basic reproduction number) and probability of establishment of RVF in the EU (the chance for RVF to be further transmitted, linked to the presence of susceptible hosts and conditions), along the relevant pathways of introduction of the disease.

First, the possible pathways for RVF introduction were reviewed. The role of infected animals, infected vectors, contaminated products and infected humans was considered; and it was concluded that the movement of infected animals (legally traded or uncontrolled movements) and of infected vectors by active flight or their passive transport when shipped by flights, containers or road transport could be considered as plausible pathways of introduction and were therefore further considered in the assessment.

The rate of RVFV entry into the EU through the entry of infected animals is assessed as 'very low' (considering the scale of qualitative assessment of MINTRISK, which corresponds, in the worst-case scenario, to one entry every 500 years), this is linked to the strict trade rules on animal import, which basically prevent any import of animals from RVF-affected countries, whereas through the introduction of infected vectors is considered 'low' for France (median: 0.000282 entries/year; CI: $8.9*10^{-7}$; 0.056), Germany (median: 0.000251 entries/year; CI: $3.9*10^{-7}$;0.11) and the Netherlands (median: 0.000251 entries/year; CI: 10^{-6}; 0.056), due to the greater number of connections by air and sea transports with African RVF-infected countries. Due to the level of uncertainty, other countries (Cyprus, Denmark, Luxembourg, Malta, Portugal) showed greater rates of entry of vectors (up to 0.06 entries per year) when the upper 95% confidence values are considered. This level of uncertainty is linked to the number of air and sea connections between affected countries and MSs, especially the maritime connections which generate higher uncertainty for the survival of mosquitoes at the destination.

For all MS, the level of transmission (referred as the R0, basic reproduction number) has been assessed as 'moderate'. This is linked to the presence of RVF competent vectors in all MS, the same estimated value of the basic reproduction ratio for all MSs and full susceptibility of animal hosts in all MS.

The probability of the establishment of RVFV transmission, once introduced, varies among the EU MS according to the introduction pathway considered: for the introduction through infected animals, a 'very high' probability (median 0.28, confidence interval, CI: 0.11–0.70) of RVFV transmission has been estimated for Greece, Malta and Portugal, 'high to very high' for Cyprus (median: 0.1, CI:0.02–0.35) and Italy (median: 0.1, CI:0.02–0.35); 'high' probability is considered for Belgium (median: 0.028, CI:0.01–0.071) and the Netherlands (median: 0.028, CI:0.011–0.071); 'moderate to high' for Croatia (median: 0.01, CI:0.002–0.039) and France (median: 0.01, CI:0.002–0.035. For the introduction through infected vectors, a 'very high' probability of RVFV transmission is assessed for Belgium, Greece, Malta and the Netherlands, 'high to very high' for United Kingdom, a 'high' probability is reported for Luxembourg, Portugal, and 'moderate to high' for Cyprus, Ireland, Italy. The differences

observed between probability estimates according to the two introduction pathways (animal or vector) are mainly due to differences in host density among the countries and the climatic conditions, which are inputs for the estimation of probability of the first transmission step following the introduction of infected vectors.

For the overall rate of introduction of RVF into the EU, through the animal pathway, the risk of RVF introduction is very low for all the EU MSs (less than 0.002 epidemics/year, meaning at least one epidemic in 500 years), given the strict health policies in place in the EU on the import of live animals from RVF-infected Third Countries and due to the long distance between the countries actually infected by RVF and the EU borders. For the vector pathway of introduction, the risk is very low for the great majority of MSs, but it is very low to low, when considering the median values, for Netherlands with 0.0044 epidemics/year (CI: $2.51*10^{-5}$; 1.58), meaning one epidemic every 227 years, followed by Malta with 0.0025 epidemics/year (CI: $5.62*10^{-6}$; 0.1.25), Belgium and Greece (0.0014 epidemics/year, CI: $4.47*10^{-6}$; 0.39, one epidemic every 700 years). In the worst-case scenario, and considering the uncertainty around these values (upper confidence intervals), some MS may have higher risk of RVF introduction (0.04 epidemics/year for Belgium, Greece, Luxemburg, Portugal and UK), and Netherlands and Malta may have one epidemic per year. This is mainly linked to the number of connections by air and sea transports with African RVF-infected countries. Considering the four EU regions (northern, southern, western and eastern EU), all of them are categorised as having a very low risk of introduction of RVF, for the Southern region a median of 0.002 epidemics/year (CI: $1.84*10^{-4}$–0.028), in the Western region 0.002 epidemics/year (CI: $1.35*10^{-4}$–0.03), in the Northern region 0.00086 epidemics/year (CI: $1.22*10^{-5}$–0.0205), in the Eastern region $2.8*10^{-5}$ epidemics/year (CI: $5.71*10^{-7}$–0.0011).

From the above conclusions, the following can be recommended. Considering the possible future source of risks represented by the spread of infection into new areas closer to the EU borders, it is of paramount importance for the EU to establish and maintain a close collaboration with North African and Middle Eastern countries in the surveillance of possible introduction of RVF from currently infected areas, as well as to carefully monitor the evolution of the epidemics in African countries.

Although the EU territory does not seem to be directly exposed to an imminent risk of RVFV introduction, the evolutions observed in the global situation of RVF occurrence, the risk of further spread of infection into countries closer to EU borders and the risks linked to the possible introduction of infected vectors, suggest EU authorities should strengthen, improve and harmonise their surveillance and response capacities as well as their scientific and technical expertise to be better prepared in case of RVFV introduction.

Considering the higher risk of introduction associated with the introduction of infected vectors, it is recommended to integrate the surveillance systems already in place in the EU for invasive mosquitoes, taking into account the main possible points of entry of RVFV-infected vectors. Particular attention should be given to those countries that receive major air and sea traffic from RVF-affected countries.

Disinsection procedures (spraying insecticides) in flights are compulsory in some cases and widely recommended by WHO and IATA. However, data about the efficacy of the treatments conducted in airplanes and ships in order to avoid the entry of vectors arriving from RVF-affected countries, are currently lacking.

Finally, considering a possible introduction of RVFV in the EU, information about the potential mosquito vector species associated with livestock premises and the surrounding environment will be essential to develop adequate protocols for vector control.

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1. Introduction

1.1. Background and Terms of Reference as provided by the European Commission

General introduction and background information

Rift Valley Fever (RVF) is a disease affecting primarily domestic and wild ruminants (cattle, sheep, goats), and camels. RVF is caused by a single-stranded RNA virus of the genus Bunyaviridae.

RVF is a vector-borne disease, transmitted primarily through various species of vectors (mainly hematophagous mosquitoes). Certain species of vectors (e.g. Aedes mosquitoes) may act as reservoirs of the disease during inter-epidemic periods thanks to their potential for transovarian (vertical) transmission of the virus to their eggs. As a result, new generations of RVFV-infected mosquitoes may hatch from infected eggs, especially in periods of favourable conditions (e.g. high rainfalls).

Susceptible animals are infected primarily by vector bites. Clinical signs range from sudden death or abortion to mild, non-specific symptoms, depending on the virulence of the virus strain and the species, breed and age of the affected animals. Mortality may reach 70–100% in lambs and kids, and 20–70% in adult sheep and calves. Abortion rates may reach 85–100% within the affected herds. RVF in camels can cause abortions and neonatal deaths. Infected wild ruminants usually do not show any clinical signs.

Humans can become infected by the RVF virus (RVFV), through the bites of vectors, by contact with infected animals and animal materials (blood, discharges, abortion materials etc.) or by consumption of untreated animal products (meat and milk). No human-to-human transmission has been recorded to date. About 50% of infected humans have no clinical signs while others may experience flu-like symptoms. A small percentage may develop severe clinical forms, involving haemorrhagic fever with hepatic disease, meningoencephalitis or ocular complications. The total case fatality rate varies between different epidemics (overall less than 1% in those documented).

To date, no RVF outbreaks in humans or animals have been reported in continental Europe or countries sharing land borders with the continental areas of the EU. The closest RVF evidence available are limited to serological findings from retrospective studies, carried out in Turkey, using blood samples collected from camels, gazelles and buffaloes from 2000 to 2006.

Currently, the disease is endemic in large areas of Southern and Eastern Africa, where outbreaks of RVF occur periodically (e.g. every few years), in seasons when weather conditions favour competent vectors. In recent decades, large RVF epidemics have occurred in Egypt (1977-78, 1993, 2003), Mauritania (2010, 2012, 2015), Madagascar (2007-2009), Comoros (2007) and elsewhere in the African continent (Kenya, Somalia, South Africa, Sudan, Senegal etc.). Egypt and Libya currently marks the northernmost limit of RVF spread. The disease moved outside the African continent for the first time in 2000, into the Arab peninsula (Saudi Arabia and Yemen).

On 5 April 2017, EFSA, following a request from the Commission, adopted a scientific opinion on 36 vector-borne diseases, including RVF. The opinion concluded that the risk of introduction of RVF in the EU was estimated to be very low based on a semi-quantitative method (modified MINTRISK model).

In Mayotte, a French department in the Indian Ocean, close to the Union of the Comoros islands and Madagascar, human cases of RVF were detected for the first time in 2007. Retrospective serological studies demonstrated the presence of RVF in livestock since 2004 (serological evidence). Until recently, the disease appeared to be in remission with no new human cases detected since 2011. However, in 2018, RVF reappeared in Mayotte and between 22 November 2018 and 14 March 2019, more than 101 human cases and more than 60 outbreaks in ruminants have been reported.

In response to the RVF resurgence, the competent authorities of Mayotte have been implementing surveillance and biosecurity measures, coupled with vector control/protection measures, aiming to limit the overall disease spread and prevent animal-to-human transmission. In addition, movements of ruminants and raw meat and milk thereof, originating from Mayotte, have been prohibited.

The Commission is empowered to adopt delegated acts supplementing the rules laid down in Part III of Regulation (EU) 2016/429 on transmissible animal diseases (Animal Health Law) on disease control measures for listed diseases as referred to in point (a), (b) and (c) of its Article 9 (category A, B and C diseases). Therefore, a draft Commission Delegated Regulation laying down rules for the prevention and control of certain diseases has been developed and the draft is in consultation.

The rules laid down in the above-mentioned draft Commission Delegated Regulation are largely 'taking over' the rules currently in force concerning the disease control measures in the event of animal diseases with serious effects on the livestock as they have proven to be effective in preventing

the spread of those diseases within the Union. Consequently, animal disease control measures laid down in existing Directives will be, to the extent that not already done by the Animal Health Law, replaced by the rules provided in that Delegated Regulation. This is also the case of Directive 92/119/EEC which currently provides for measures to apply in the event of occurrence of certain diseases. This includes Rift Valley fever, which is in accordance with Commission Implementing Regulation (EU) 2019/1882, categorised as Category A disease.

In this regard, the existing rules of Directive 92/119/EEC will cease to apply, in particular for Rift Valley fever, as from the date of application of the Animal Health Law and its complementing legislation, i.e. from 21 April 2021. The proposed measures for the prevention and control of RVF should be assessed in order to ensure that they are updated based on the latest scientific knowledge in this new set of legislation.

Terms of Reference

1. RISK OF ENTRY OF RVF INTO THE CONTINENTAL PARTS OF THE EU

    1.1 Provide an update of the global epidemiological situation in relation to RVF with emphasis on areas posing a higher risk for the EU.
    1.2 Provide an updated assessment of the overall risk of introduction of RVF (combined rate of entry, vector transmission and establishment), separately for each one of the EU regions potentially at risk, as specified in the 2017 EFSA scientific opinion on Vector-borne diseases (VBD).
    1.3 Provide a separate risk assessment of the risk of introduction of RVF for specific Member States that may be at particular risk.

2. IMPACT OF RVF IN THE DEPARTMENT OF MAYOTTE AND RELEVANT CONTROL MEASURES

    2.1 Assess the probability of overwintering of RVF in the department of Mayotte as well as the risk of RVF spreading from Mayotte to other areas including other French departments in the Indian Ocean or Metropolitan France.
    2.2 Assess the impact of the disease (as defined in the 'VBD opinion'), with emphasis on animal health and farm production in Mayotte from the time of its initial occurrence to date.
    2.3 Assess the possible short and long-term effectiveness, of different control measures, in eliminating or reducing the disease impact in Mayotte (as per TOR 2.2 above), namely:

        2.3.1 Stamping out of RVF outbreaks;
        2.3.2 Establishment of a protection and a surveillance zone around RVF outbreaks;
        2.3.3 Biosecurity measures, as the ones currently in place in Mayotte, coupled with personal sanitary protection measures related to human–animal contact, including measures to prevent consumption of potentially infected meat and milk;
        2.3.4 Vector control and protection measures;
        2.3.5 Vaccination of livestock

    2.4 Assess the possible effectiveness of different surveillance strategies in animals that may be used for RVF detection and possible prediction of RVF recurrence in Mayotte in the future, in view of the diagnostic methods currently available.

3. SURVEILLANCE AND CONTROL MEASURES FOR RVF [IN CASE OF OCCURRENCE OR HIGH RISK OF RVF INCURSION IN EUROPE]

    3.1 In case of high risk of RVF introduction in Europe assess and describe the surveillance measures necessary to ensure early detection of the disease
    3.2 In case of RVF occurrence in Europe, assess the effectiveness of the main available disease prevention and control measures for RVF, including the relevant measures provided for in the draft Commission Delegated Regulation on rules for the prevention and control of certain listed diseases under Part III of Regulation (EU) 2016/429 on transmissible animal diseases (Animal Heath Law9), namely their potential to:

        — limit the geographical spread of the disease
        — reduce the number of outbreaks
        — reduce the overall impact of the disease being present in an area for prolonged periods (e.g. in case overwintering is possible)

In particular, assess the feasibility, availability and effectiveness of:

3.2.1 the general measures set out in the enacting terms of Part I and II of draft Commission Delegated Regulation
3.2.2 the disease-specific measures set out in Annexes I to X to draft Commission Delegated Regulation
3.2.3 vaccination of listed species, including assessment of possible:

— risk mitigating measures necessary to be put in place for animals and products of animal origin thereof, following vaccination
— surveillance performed after vaccination.

1.2. Interpretation of the Terms of Reference (if appropriate)

It was agreed with the European Commission to address the ToRs in three scientific opinions to be delivered according to the following deadlines:

- January 2020 for the ToRs 1.1, 1.2 and 1.3
- March 2020 for ToRs 2.1 and 2.2
- September 2020 for ToRs 2.3, 2.4 and 3.

In the first present opinion, the term of reference related to the risk of introduction of RVF into EU will be addressed by providing an assessment of the rate of entry, the risk of vector transmission and the probability of establishment of RVF as well as the combined overall risk of introduction of RVF first for each single Member State, and then for the EU regions as in EFSA Panel on Animal Health and Welfare (2017). This allows for a more complete and detailed scenario of risk of introduction of RVF into EU, which is more useful for risk management purposes, since the risk is assessed for all MSs, and not only for those at risk.

2. Data and methodologies

2.1. Data

Previous scientific outputs of EFSA on RVF (EFSA, 2005, 2013), outbreak and trade data were collected in order to provide a description of the updated epidemiological situation and for the analysis of the risk of introduction of RVF.

2.1.1. Epidemiological data

Epidemiological data of RVF outbreaks were obtained by OIE and ADNS for the animal outbreaks, for African countries and MS (Mayotte, France), respectively, and from WHO for the notifications of the human outbreaks.

2.1.2. Trade, travel and temperature data

Data related to the trade movement of large and small ruminants were collected from EUROSTAT and UN COMtrade.[1]

Data related to flights, passengers, containers shipped on sea and road transport were obtained by EUROSTAT.

Temperature data of 2013–2018 were obtained by the AgriCast resources Portal[2] of the EU Commission interpolated on a 25x25 km grid.

Other data and information sources considered were the REMESA network for North Africa and Middle East countries as well as direct contact with OIE regional representatives and Chief Veterinary Officers (CVOs) from France, Egypt, Chad, Mali, Jordan, Lebanon and Saudi Arabia.

[1] UN Comtrade is a repository of official international trade statistics and relevant analytical tables. It provides free access to detailed global trade data through API.
[2] https://agri4cast.jrc.ec.europa.eu/DataPortal/Index.aspx?o=

2.2. Methodologies

2.2.1. ToR 1.1: Global epidemiological situation in relation to RVF

For the first ToR about the update on the global epidemiological situation of RVF, both descriptive statistics and information from the literature were used. The approach used was to update the information provided in the RVF story map published by EFSA (link).

2.2.2. ToR 1.2 & 1.3: Risk of introduction to EU

The risk of introduction of RVF into each of the MSs and each of the EU regions is assessed by the general framework of EFSA VBD_RISK model developed in MINTRISK as presented in EFSA Panel on Animal Health and Welfare (2017), with some additional improvements.

The MINTRISK model is a tool to assess the level of introduction, transmission and impact of vector-borne diseases. MINTRISK stands for Method to INTegrate all relevant RISK aspects; it is a tool developed in Excel and Visual Basic. A web-based version with a central database and using Csharp for underlying calculations has been created for practical use and access.[3] This tool allows for a systematic, semi-quantitative risk assessment, which can be used for risk evaluation, risk comparison and risk ranking of possible vector-borne diseases of livestock.

The MINTRISK approach to assess the overall risk of pathogen/disease introduction into the EU involves four steps as follows (Figure 1):

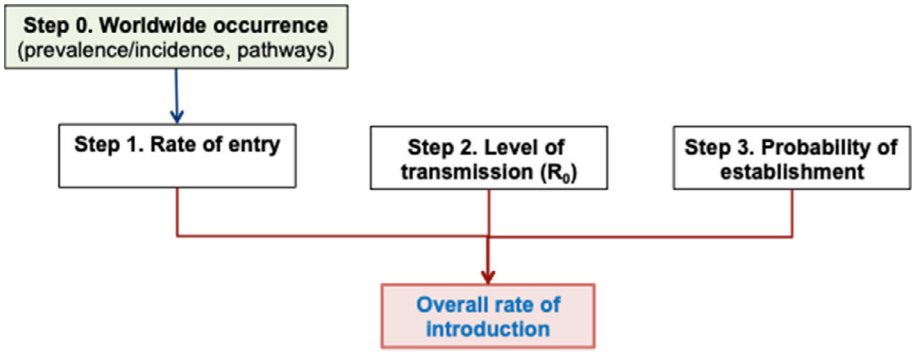

Figure 1: Steps for the MintRisk approach to assess the overall risk of pathogen/disease introduction into the EU

The possible pathways of introduction of RVF were discussed and selected based on literature and expert knowledge. These are discussed in Section 3.2.1.

For each of the selected pathways, the probability of each step of the risk pathway was calculated. First, the occurrence, rates of entry (number of entries/year), level of transmission (R0, basic reproduction number) and probability of establishment were calculated separately, and then these three values were combined into an overall rate of introduction (number of epidemics/year).

The calculation of the probability of each step for each pathway and each MS was based on the answers to a set of questions to be addressed. Possible answers were qualitative categories (each with its own underlying quantitative translation, see Annex A.4) associated with a level of the uncertainty (low, moderate, high[4]). A Monte Carlo simulation was used to determine the overall uncertainty in the probability for each step of the pathway and for the overall probability. For most of the questions, the answer categories were given on a logarithmic scale and the outcomes were always expressed on a logarithmic scale. The questions to be answered for each step are listed in Section 2.2.2.2.

The successive steps to assess the overall risks of introduction are as follows:

[3] https://www.wecr.wur.nl/mintrisk/ModelMgt.aspx

[4] Three uncertainty levels can be selected to describe the certainty when answering the questions in the MINTRISK model. The model will sample a value from triangular distributions with different ranges around the answer category according to the chosen uncertainty level for a 'moderate' answer category. The ranges around the answer category are +/ 0.1 for low, +/ 0.3 for moderate and +/ 0.5 for high uncertainty (EFSA Panel on Animal Health and Welfare, 2017).

- **Rates of introduction for MSs:**

For each MS 'n' (with $n = 1, N$ total MSs), the overall rate of introduction is given by,

$$R_n = \sum_{p=1}^{\text{all pathways}} R_{n,p}$$

where $R_{n,p}$ is the rate of introduction for each pathway p. For each MS and each pathway, the rate $R_{n,P}$ is obtained using MINTRISK (see Annex A.5).

- **Spatial model of rates of introduction:**

The aim is to consider the *N* heterogeneous introduction rates R! all together at the geographical level and combined them at the regional scale. To this end, a Bayesian CAR (conditional autoregressive) model that takes into account the geographical heterogeneities of the R_n is developed as follows,

  - Smooth the Rn as $Rn \rightarrow \tilde{R}_n$
  - Simultaneously compute the introduction rates at the regional scale as, $R_{region} \rightarrow \tilde{R}_{region}$ where

$$R_{region} = \sum_{n=1}^{\text{all MSs} \in \text{region}} R_n$$

in which the summation stands for all MSs belonging to the EU region under consideration.

- **Outcomes:**

  - **ToR 1.3:** Distributions of rates of introductionR! for each MS, reported as: median of R_n + 95% CI [2.5%; 97.5%] percentiles.
  - **ToR 1.2:** Distributions of rates of introduction R_{region} for each EU region, reported as: median of R_n + 95% CI [2.5%; 97.5%] percentiles.

The four EU regions considered in the (EFSA Panel on Animal Health and Welfare, 2017) are:

- Northern EU (N-EU): Lithuania, Denmark, Latvia, Ireland, Finland, Estonia, Sweden, United Kingdom;
- Southern EU (S-EU): Spain, Greece, Malta, Italy, Croatia, Slovenia, Portugal, Cyprus;
- Western EU (W-EU): Belgium, the Netherlands, Luxembourg, France, Germany, Austria;
- Eastern EU (E-EU): Hungary, Poland, Czechia, Bulgaria, Slovakia, Romania.

2.2.2.1. Risk of introduction of RVFV by vectors

Vectors infected with RVFV from endemic countries can be introduced into an MS by different means. In this opinion, we are only considering passive transport of vectors by means of transport (mainly aerial and sea transportation) since other vector pathways, such as passive transport of vectors by winds and active movement of the insects, were assumed to be negligible considering the long distance between endemic countries included in this opinion and the EU MS.

The origin of introduction of RVFV-infected vectors to EU MS was focused only on those countries where RVF outbreaks either in animals or humans were detected from 2006 to 2019 (Table 1).

Table 1: Countries that experienced at least one outbreak of RVF in human or animals since 2006 until 2019 according to OIE and WHO, with indication of the availability of data (Y is for available) for air, sea and road transportation to the EU MS

	Country	OIE	WHO	Air	Sea	Road
1	Botswana	3				
2	Central African Republic		1			
3	Chad	1				
4	Comoros	6				
5	Democratic Republic of Congo	3				
6	Egypt*			Y	Y	
7	Gambia		1		Y	

	Country	OIE	WHO	Air	Sea	Road
8	Kenya	50	5	Y	Y	
9	Madagascar	7	5	Y	Y	
10	Mali	1	1	Y		
11	Mauritania	12	14		Y	
12	Mayotte (France)	3	1			
13	Mozambique	21			Y	
14	Namibia	15			Y	
15	Niger	1		Y		Y
16	Nigeria	4			Y	
17	Saudi Arabia	1		Y	Y	
18	Senegal	5		Y	Y	
19	South Africa	677		Y	Y	
20	South Sudan	1				
21	Sudan	6	1		Y	
22	Uganda	4				
23	Rwanda	8		Y		
24	Swaziland	2				
25	Tanzania		5			
26	Yemen*					

*: Egypt and Yemen are included since they experienced outbreaks before 2006 but they are endemic countries.

A list of the vector species present in the selected countries was elaborated where the different species of vectors were ranked according to their ability to be introduced into the EU based on their ecology and vector capacity (Vectornet External Report, ref to be added). For example, vector species that are able to breed in man-made containers were considered as having a higher risk to be transported. From the list of selected vector species present in RVFV endemic countries, the risk of introduction into EU MS countries was estimated using the MINTRISK model (section above), where the risk of introduction of a RVFV vector species into a specific MS was estimated considering separately the frequency of passive movement of vectors (air and sea transportation; road transportation was not considered due to the low number of lorries driven from RVFV endemic countries to Europe and lack of data from most of the countries), the probability of survival during the transport (as a function of transport duration, Annex A.3) and the probability of moving RVFV-infected vectors. For estimating the frequency of passive transport, data on the number of flights and number of container shipments for 2016–2018 were considered, combined with the probability of finding a mosquito in any of those means of transport (Annex 8.1). The prevalence of infected vectors was estimated according to the references published in the different RVFV endemic countries and reviewed by Braks et al. (2017). For those countries where references were not available, the prevalence of infected vectors was extrapolated from those neighbouring countries that share the same species of vectors.

For the probability of establishment (first and second step of transmission when and if an infected vector or host is introduced), the climatic situation in each MS has been considered by assigning a coefficient calculated as the proportion of days above 9.6°C in the 5 years 2013–2018 in each MS.

2.2.2.2. MINTRISK questions and assignment of category values

The part of the MINTRISK model related to risk of introduction is structured in four components, i.e. worldwide occurrence of the disease, rate of entry, level of transmission and probability of establishment. For RVF, two pathways have been considered, the animal and vector pathways. For each component, a set of questions need to be answered with a value chosen from a scale given by the model and a related level of uncertainty (low, moderate, high). The description of the methodology used and the reasoning to assign the different values is given below.

STEP 0: WORLDWIDE OCCURRENCE

1. What is the relative size of the infected area to the total area addressed?

This aims at estimating the fraction of the animal population (expressed as an area) which is at risk during the epidemic.

- Reasoning: the area considered is the sum of the area of the affected countries in 2016–2019 (see Section 3.1.2) plus the area of endemic ones (Central African Republic, Chad, Gambia, Kenya, Mali, Mayotte, Mozambique, Niger, South Africa, South Sudan, Sudan, Uganda, Rwanda, Nigeria, Egypt, total area 10.09 million square km) divided by area of African continent (30.37 million square km), which makes 0.33.
- Value set in MINTRISK: > 0.3, very large, for both pathways and all MSs (scale: very small: < 0.01; small: 0.01–0.03; moderate: 0.03–0.1; large: 0.1–0.3; very large: > 0.3).
- Uncertainty: low.

2. How likely is it that the disease will not be notified to OIE?

This is the probability of no notification, despite an epidemic. In MINTRISK, the values range is very unlikely: < 0.2 (20%); unlikely: 0.2–0.9; moderate: 0.9–0.99; likely: 0.99–0.999; very likely: > 0.999)

- Value set in MINTRISK: Very unlikely, < 0.2, for both pathways and all MSs, same approach was taken in (EFSA Panel on Animal Health and Welfare, 2017).
- Uncertainty: moderate. There are big areas in the sub-Saharan region without much information.

3. What is the duration of undetected spread?

- reasoning: As indicated in (EFSA Panel on Animal Health and Welfare, 2017), many factors contribute to the detection of a disease in the short term, such as the surveillance capacities, how the epidemics develop, if human cases are involved, etc. It was considered that a reasonable value could be 1–3 months, the same approach was taken as in the (EFSA Panel on Animal Health and Welfare, 2017).
- Value set in MINTRISK: short (0.1–0.3 year), for both pathways and all MSs (scale: very short: < 0.1 year; short: 0.1–0.3 year; moderate: 0.3–1 year; long: 1–3 year; very long: > 3 year).
- Uncertainty: moderate.

4. What is the frequency with which the epidemic occurs in the addressed area?

- reasoning: see the number of epidemics per year in Africa (Section 3.1.2)
- value set in MINTRISK: moderate, 0.3–1 per year, for both pathways and all MSs (scale: very low: < 0.1 per year; low: 0.1–0.3 per year; moderate: 0.3–1 per year; high: 1–3 per year; very high: > 3 per year).
- Uncertainty: low.

5. How high is the prevalence of the infection in host animals or vectors in the region in the end of HRP of an epidemic in that region?

- MINTRISK scale: very low: < 1E-4; low: 1E-4 - 0.001; moderate: 0.001–0.01; high: 0.01–0.1; very high: > 0.1.
- Animal pathway: number of cases/susceptible in 2016–2019, considering the number of cases/susceptible as from outbreak data from OIE in the period 2016–2019; this would be 1E-4 - 0.001, thus 'low' in MINTRISK; uncertainty: low.
- Vector pathway: based on the review by Tantely et al. (2015), mean value of 53 values reported in different countries and in different species, mean: 67% with SD 29.74, would be in the category very high, including filed and laboratory trials on vector competence; while, according to a literature review presented in Braks et al. 2017, the average minimum infection rate in RVF vectors is 3.54% (SD 8.14) considering only field data, falling in the MINTRISK category high, uncertainty: moderate. For this assessment, the value of prevalence from field data is considered as the most appropriate.

STEP 1: RATE OF ENTRY

6. **What are the average numbers /volumes of animals/vectors/commodities moved along the pathway per year?**

- Scale: (minimal: < 100; minor: 100–10^3; moderate: 10^3–10^4; major: 10^4–10^5; massive: > 10^5)
  - Animal pathway: the category of the MINTRISK is assumed to be 'minimal', see Section 3.2.1.1, for all MS.
    - Uncertainty: low.
- Vector pathway: number of mosquitoes moved per maritime transport and flights per year from African countries towards MS, see Vectornet report and Annex A.3.
    - Uncertainty: to assign the uncertainty category for Mintrisk see Annex A.1.

7. **What is the probability of passing through the preventive/control measures before/at transport?** (very low: < 0.001; low: 0.001–0.01; moderate: 0.01–0.1; high: 0.1–0.8; very high: > 0.8)

This is the probability (P) of being removed from import due to risk prevention measures, such as testing and quarantine for animals or insecticide treatment for vectors.

- **Animal pathway**: as in (EFSA Panel on Animal Health and Welfare, 2017):
  - SE: -Sensitivity_diagTest2: 93%
  - D1: Duration kept on the holding before dispatch (days): 40
  - D2: Duration of quarantine at border (days): 30
  - Det1: Median of first detection of virus (days): 1
  - Det2-Median of last detection of virus (days) : 2
  - IP: Infectious period of the host:1

    P = 1−Se*EXP(−(D1 + D2)/(Det1 + Det2)

  - for all MS: <0.001, very low
  - Uncertainty: low
- **Vector pathway**: controlled trials about the efficacy of treatment in flights showed 100% efficacy (Russell and Paton, 1989). However, there is little information about the efficacy of disinsection in real conditions, despite it being highly recommended by (WHO, 2012, 2018) and (International Air Transport, 2018). Aspects such as resistance to insecticides are also of importance, since intercepted *Ae. aegypti* mosquitoes detected at international ports in New Zealand and Australia had point mutations that confer resistance to synthetic pyrethroids (Ammar et al., 2019). In general, there is no consensus among authors in regard to the efficacy of disinsection conducted in airplanes to avoid the entry of transported mosquitoes, since it would depend on the countries whether or not air travel companies require the application of the insecticide treatment, and furthermore, there are different legislations in terms of the type of products (Gratz et al., 2000; Grout, 2015; Mier-y-Teran-Romero et al., 2017). For example, Scholte et al. (2008) considered that since no mosquitoes were found in those companies that used insecticides, the control method could be considered as effective. Similarly, Lounibos (2002) considered that insecticide applications, either on the ground or in-flight, are effective based on the works from Russell & Paton (1989), but admits that systematic disinsection is rare and therefore not avoiding the establishment of the majority of vectors arriving on airplanes. On the contrary, Brown et al. (2012) considered that despite the effort on airplane disinsection, it would not be sufficient to avoid the risk of mosquitoes from entering the United Kingdom, since for example *Culex* mosquitoes are frequently in the cargo hold where traditional disinsection is usually not conducted or can be less efficacious (Whelan et al., 2012).
- Thus, according to the information currently available, the probability for vectors to be controlled before or at transport can be considered as 'moderate', with high uncertainty.

8. **What is the probability that a viable VBD-agent is still present upon arrival in the area at risk?**

This is the probability of survival of the infection (P2), given the mode and duration of transport.

- **Animal pathway**:
  - EXP(-duration of journey/(median first detection + infectious period))
  - duration of infection: min = 1 day and max = 3 days
  - duration of journey: min = 1 day and max = 5 days
  - P2 (mean) = 0.301 (CI: 0.124; 0.536)
  - MINTRISK range: low (0.1–0.8)
  - Uncertainty: low
- **Vector pathway**:
  - RVFV is viable in a surviving vector and the survival of mosquitoes depends on the length of trip at sea (4–15 days).[5] This is weighted for flights where the survival is always very high compared to sea transport per each MS. See calculation in Annex A.2.
  - Uncertainty: in order to assign the uncertainty category for MINTRISK:

    X = (Upper CI_Value – LowerCI_Value)/(2 × Value),
    then: X < = 0.1 –> Low; 0.1 < X < = 0.3 –> Moderate; 0.3 < X –> High

STEP 2: LEVEL OF TRANSMISSION

9. What is the distribution of the vector in the area at risk?

- Categories in MINTRISK: absent; present, absent or unknown.
- Value set: *present* for all MSs (Wint et al., 2020).
- Uncertainty: low.

10. What is the estimated value of the basic reproduction ratio?

- Scale in MINTRISK: very low: < 0.3; low: 0.3–1; moderate: 1–3; high: 3–10 very high: > 10.
- The estimated value ranges between 2.3 and 6.8 (which corresponds to *moderate to high* in MINTRISK), with uncertainty category 'moderate' (Braks et al., 2017).

11. Which fraction of the host population is susceptible (i.e. not protected from infection by routine vaccination or previous exposure)?

- Scale in MINTRISK: very low: < 0.03; low: 0.03–0.1; moderate: 0.1–0.3; high: 0.3–0.8; very high: > 0.8.
- Reasoning and value: 100% RVF host animals in EU would be susceptible to RVF.
- Uncertainty: low.

STEP 3: probability of establishment

12. What is the probability of infecting a first local (indigenous) vector or host, given the pathway of entry and the expected region and time of entry? [1st transmission step]

- Scale in MINTRISK: very low: < 1E-4; low: 1E-4 - 0.001; moderate: 0.001–0.01; high: 0.01–0.1; very high: > 0.1.
- Reasoning: given one infected vector or infected host enters, the probability of the first transmission step would depend on the chance of finding the respective susceptible host or vector, besides the sufficiently high temperature for the vector activity. The host density has been estimated by the number of ruminants in relation to the MS area; for the vector presence, the proportion of each MS with competent RVFV vectors has been considered (Wint et al., 2020); for the temperature, a coefficient based on the proportion of days above 9.6°C in the years 2013–2018 per each MS has been calculated. The probability for the first transmission step when an infected vector would enter has been calculated as the geometric mean of host density and temperature coefficient; while the probability for the first transmission step when an infected host would enter has been calculated as the geometric mean of vector presence and temperature coefficient. The categories for MINTRISK have been assigned according to 20th, 40th, 60th, 80th percentiles of the distribution of the geometric mean (see Annex A.3).
- Uncertainty: low.

[5] Transovarial transmission is not considered; see Section 3.1.3.3.

13. **What is the probability of infecting a first local vector (given first infection of an indigenous host) or host (given first infection of an indigenous vector)? [2nd transmission step]:**
    - Scale in MINTRISK: very low: < 0.001; low: 0.001–0.01; moderate: 0.01–0.1; high: 0.1–0.8; very high: > 0.8.
    - Reasoning: the probability of the second transmission step would depend on the chance of finding at the same time a susceptible host and vector and the seasonality for the vector activity. The same approach as for point 12 has been used, but the three values have been combined, the geometric mean of the three values (host density, vector presence and seasonality) has been computed and five categories for MINTRISK assigned according to 20th, 40th, 60th, 80th percentiles of the distribution of the geometric mean. (Annex A.3).
    - Uncertainty: low.

3. Assessment

3.1. Global epidemiological situation in relation to RVF

In this section, the most relevant information on RVF is summarised about the characteristics of the virus, the spatial and temporal distribution of RVFV and the evolution of the disease by focusing on its expansion towards Europe, diagnostic tools and vaccines.

3.1.1. Disease agent

Rift valley fever virus (RVFV) belongs to the genus *Phlebovirus*, family *Bunyaviridae* even though recently proposed to be reallocated to the family *Phenuiviridae* (Maes et al., 2018). The virion has an icosahedral symmetry with a host cell-derived bilipid-layer envelope through which virus-coded glycoprotein spikes project. The viral genome is composed of three RNA segments, L (large), M (medium) and S (small), of negative or ambisense polarity, each of them contained in a separate nucleocapsid within the virion (Coetzer and Tustin, 2005). The genome segments encode four structural proteins: the viral polymerase (L) on the L segment, two glycoproteins (Gn and Gc) on the M segment, and the viral nucleocapsid protein (N) on the S segment (Struthers et al., 1984). RVFV Gn and Gc glycoproteins being exposed on the outer surface of the virus during infection (Huiskonen et al., 2009), are recognised by the host immune system and induce the production of neutralising antibodies. Together with the N protein, they elicit the production of RVFV-specific RVFV IgG and IgM antibodies after infection. RVFV virus additionally expresses two non-structural proteins, NSm1 and NSm2, encoded on the M segment and NSs on the S segment (Gerrard and Nichol, 2007). These non-structural proteins play important roles for pathogenesis (Vialat et al., 2000; Won et al., 2006; Gerrard et al., 2007; Bird et al., 2008). Transcription and replication take place in the cell cytoplasm.

RVFV consists of a single serotype with a limited genomic variability among the circulating strains (Bird et al., 2008).

RVFV survives in the freeze-dried form and in aerosols at 23°C under 50–85% of humidity, with 25% of the initial infectivity being retained at 1 h. The virus can be maintained several years through the egg stage of some arthropod vector species belonging specifically to the *Aedes* genus during inter-epidemic periods (lasting till 5–15 years). It can survive contact with 0.5% phenol at 4°C for 6 months (OIE, 2009).

Heat and low pH (< 6) inactivate the RVFV as is the case with lipid solvents, detergents and disinfectants. Infectivity is maintained in protein-rich medium (e.g. plasma or serum) for up to 20 h at 'room temperature' (conventionally 22°C), 8 months at 4–5°C and 8 years under a variety of (unspecified) conditions of refrigeration. Infectivity survives heating to 56°C for up to 3 h, RVFV is most stable at pH 7.0–7.8, labile at pH < 6.8 or > 8.0, sensitive to ether and bile salts, destroyed by low concentrations of formalin, or by methylene blue in the presence of light (EFSA, 2005).

Key message:

- RVFV consists of a single serotype of the genus *Phlebovirus* with a limited genomic variability among the circulating strains.
- The virus is readily inactivated by lipid solvents and acid conditions (pH < 6).

3.1.2. Spatial and temporal distribution of RVF

3.1.2.1. Worldwide distribution

Since 2006 to the present (2019), RVF spread in livestock in southern Africa, East Africa and Saudi Arabia, then outbreaks were reported in West Africa in 2010–2012 with even human cases (Mauritania). More recently, it was reported in East Africa in Kenya, Uganda, Sudan and Tanzania, and in 2018–2019, a broad epidemic was reported in Mayotte (France). The spatial and temporal distribution of the reported RVF outbreaks in animal and human populations from 2006 to October 2019 is shown in Figure 2 and in the movie map at this link https://doi.org/10.5281/zenodo.3688061.

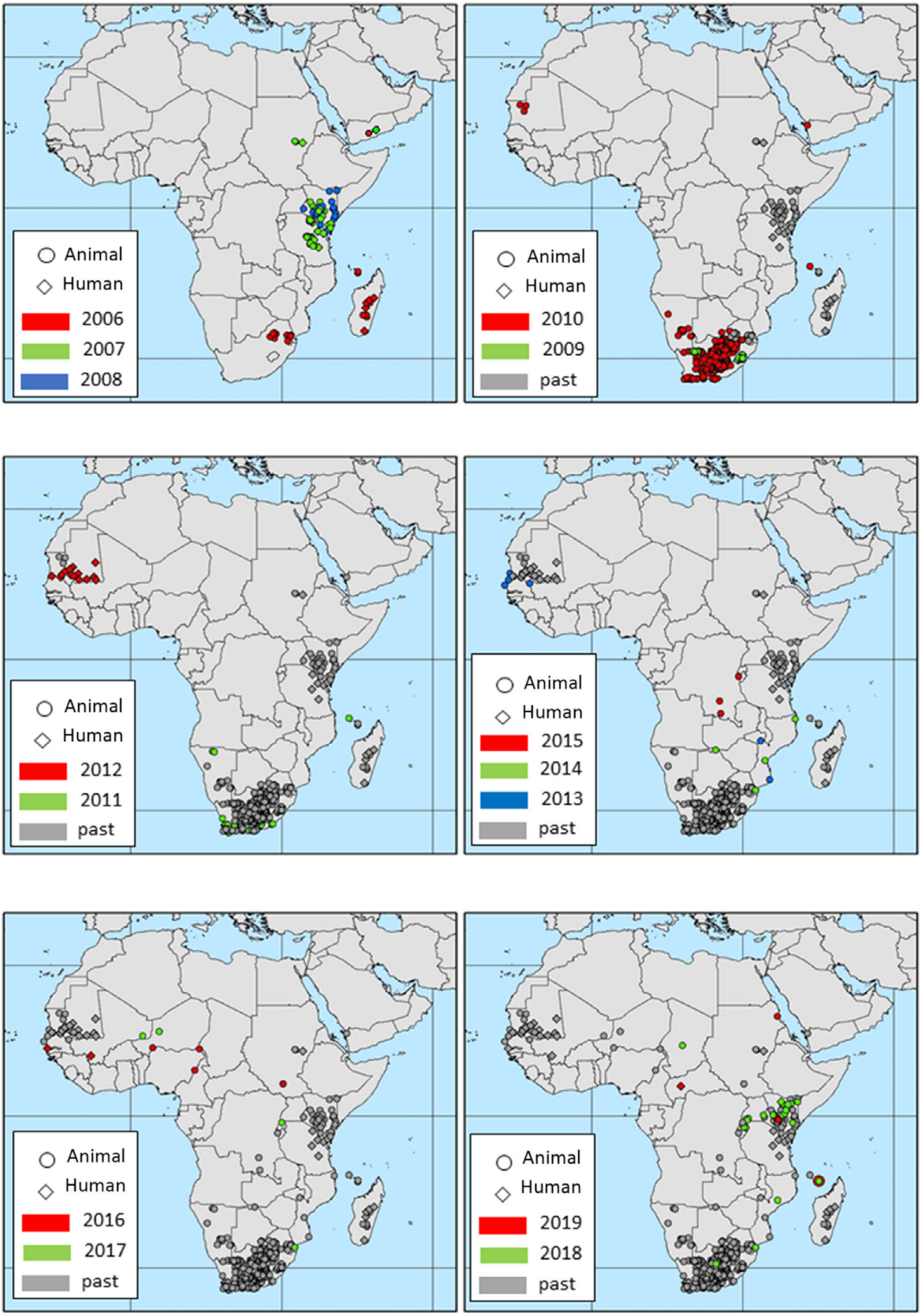

Figure 2: Temporal distribution of reported RVF outbreaks in animals and humans from 2006 to October 2019 (OIE and WHO data)

Figure 3 shows the cumulative number of years of reported presence of RVF (see also Table 2), together with the different animal species and human outbreaks.

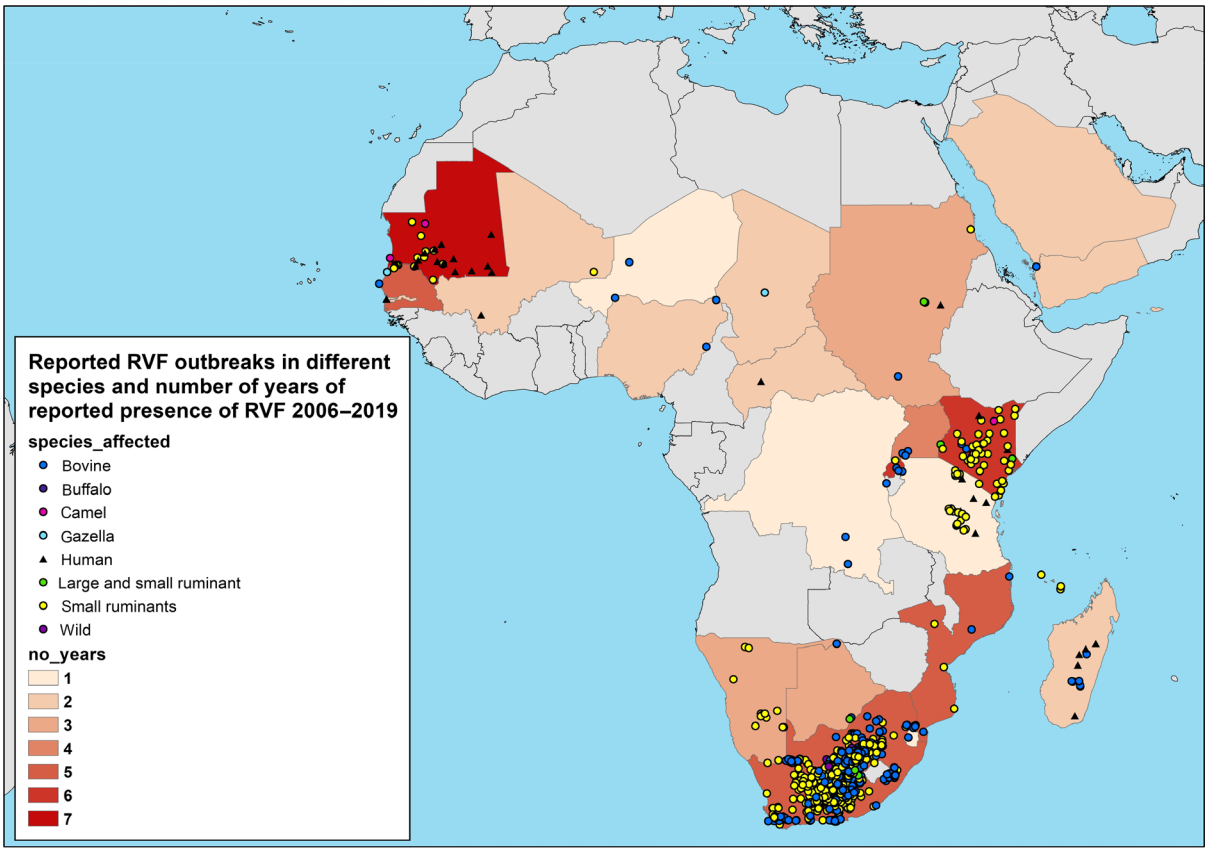

Figure 3: Number of years of reported presence of RVF and species affected in the outbreaks reported between 2006 and 2019 (OIE and WHO)

Table 2: Countries where and years when RVF outbreaks were officially notified either to the OIE and ADNS for animals or to WHO for humans, since 2000 (Sources: OIE and ADNS for animal data; WHO for human data[6]).

Country	Years of notification		TOTAL
	Outbreaks in Animals (OIE and ADNS)	Outbreaks in humans (WHO)	
Botswana	2010/2014/2017		2010/2014/2017
Central African Republic		2019	2019
Chad	2018		2018
Comoros	2008/2009/2010/2011		2008/2009/2010/2011
Democratic Republic of Congo	2012		2012
Egypt		2003	2003
Republic of Guinea	2006		2006
Gambia		2002/2018	2002/2018

[6] https://www.who.int/csr/don/archive/year/2019/en/ and https://www.who.int/csr/don/archive/disease/rift_valley_fever/en/; https://www.who.int/news-room/fact-sheets/detail/rift-valley-fever

Country	Years of notification		TOTAL
	Outbreaks in Animals (OIE and ADNS)	Outbreaks in humans (WHO)	
Kenya	2006/2007/2018/2019	2006/2007/2014/2015/2018	2006/2007/2014/2015/2018/2019
Madagascar	2008/2009	2008/2009	2008/2009
Mali	2016/2017		2016/2017
Mauritania	2006/2010/2011/2012/2013/2014/2015	2010/2012	2006/2010/2011/2012/2013/2014/2015
Mayotte (France)	2008/2018/2019	2019	2008/2018/2019
Mozambique	2007/2013/2014/2016/2018		2007/2013/2014/2016/2018
Namibia	2010/2011/2012		2010/2011/2012
Niger	2016	2016	2016
Nigeria	2017		2017
Rwanda	2012/2013/2014/2016/2017/2018		2012/2013/2014/2016/2017/2018
Saudi Arabia	2010	2000	2000/2010
Sudan	2007/2019	2007/2008/2019	2007/2008/2019
South Sudan	2017/2018		2017/2018
Senegal	2013/2014/2015/2016/2018		2013/2014/2015/2016/2018
Somalia		2006/2007	2006/2007
Eswatini	2008		2008
Tanzania	2007	2007	2007
Uganda	2016/2017/2018	2019	2016/2017/2018/2019
South Africa	2008/2009/2010/2011/2018	2010	2008/2009/2010/2011/2018
Yemen	2005/2006/2007	2000	2000/2005/2006/2007

The occurrence of major RVF epidemics has been historically considered to be linked to climatic conditions like the occurrence of the warm phase of the El Nino/Southern Oscillation (ENSO) phenomenon causing floods, increased greenness of vegetation index and emergence of mosquito vectors infecting susceptible ruminant hosts (Nanyingi et al., 2015). This would explain the multi-annual cyclic appearance of the disease in some areas of Africa, such as southern Africa and sub-Saharan Africa like in Kenya or in Mauritania. Nevertheless, in the last decade, RVF epidemics have been occurring more frequently in West Africa and in other sub-Saharan countries. This may be linked to some low-level circulation of RVFV in livestock (undetected but present and circulating), which has been observed in various countries (Rissmann et al., 2017; Clark et al., 2018).

The Centres for Disease Control and Prevention (CDC, USA), taking into consideration historical information on human and animal cases as well as the detection of RVF antibodies with different serological tests, have classified the countries according to the epidemiological situation on RVF in three classes (endemic, sporadic presence, unknown status) as it is presented in Figure 4.

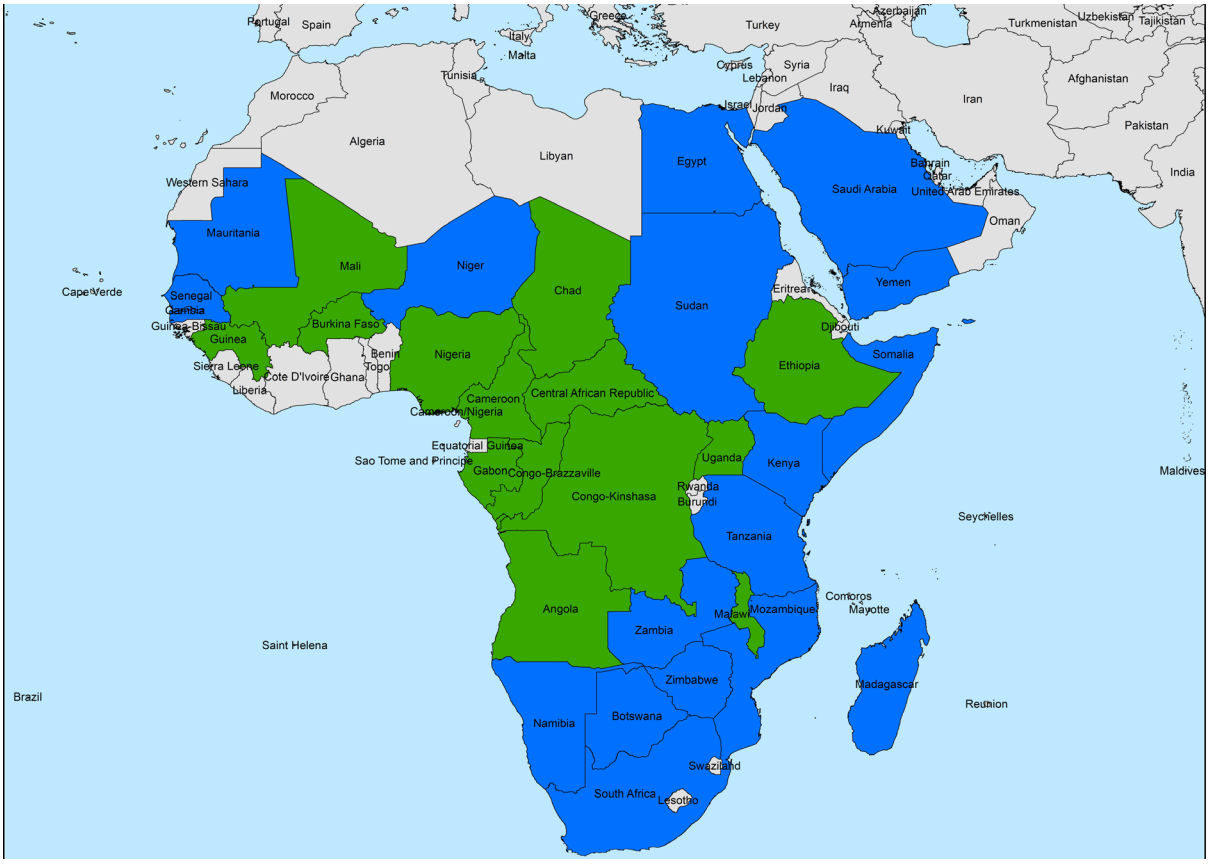

Figure 4: Amended map of CDC classification of the countries where RVF has been confirmed: (i) blue: countries reporting endemic disease and substantial outbreaks of RVF; (ii) green: countries reporting few cases, periodic isolation of virus, or serological evidence of RVF; and (iii) grey: RVF status unknown or not reported. (source: CDC[7])

From Figure 4, the most important areas at risk of representing a possible front of expansion of RVF towards Europe are Arabic Peninsula and the Middle East.

3.1.2.2. Mayotte

The Mayotte Department is a part of the French Territory belonging to the EU Territory (i.e. where EU regulations apply); therefore, French Veterinary Authorities are obliged to notify the RVF outbreaks[8] to the EU Animal Disease Notification System (ADNS),[9] according to the Council Directive 82/894/EEC.[10] The data on ADNS include only the outbreaks that have been officially confirmed and notified by the Veterinary Authorities. An outbreak can referred to more than one affected animal even in different species if they constitute a unique epidemiological unit and are identified at the same location. Up until the end of October 2019, 125 outbreaks were reported in Mayotte in ruminants (cattle, sheep, goats) (Figure 5).

[7] downloaded on 7/10/2019; https://www.cdc.gov/vhf/rvf/outbreaks/distribution-map.html

[8] Definitions of the terms outbreak and case (article 4 Directive 82/894): 'outbreak' means the holding or place situated in the territory of the Community where animals are assembled and where one or more cases has or have been officially confirmed. While 'case' means the official confirmation of any of the diseases listed in Annex I of the Directive 82/894 in any animal or carcass.

[9] ADNS, the EU Animal Disease Notification System, see http://ec.europa.eu/food/animals/animal-diseases/not-system_en

[10] Council Directive 82/894/EEC of 21 December 1982 on the notification of animal diseases within the Community http://data.europa.eu/eli/dir/1982/894/oj

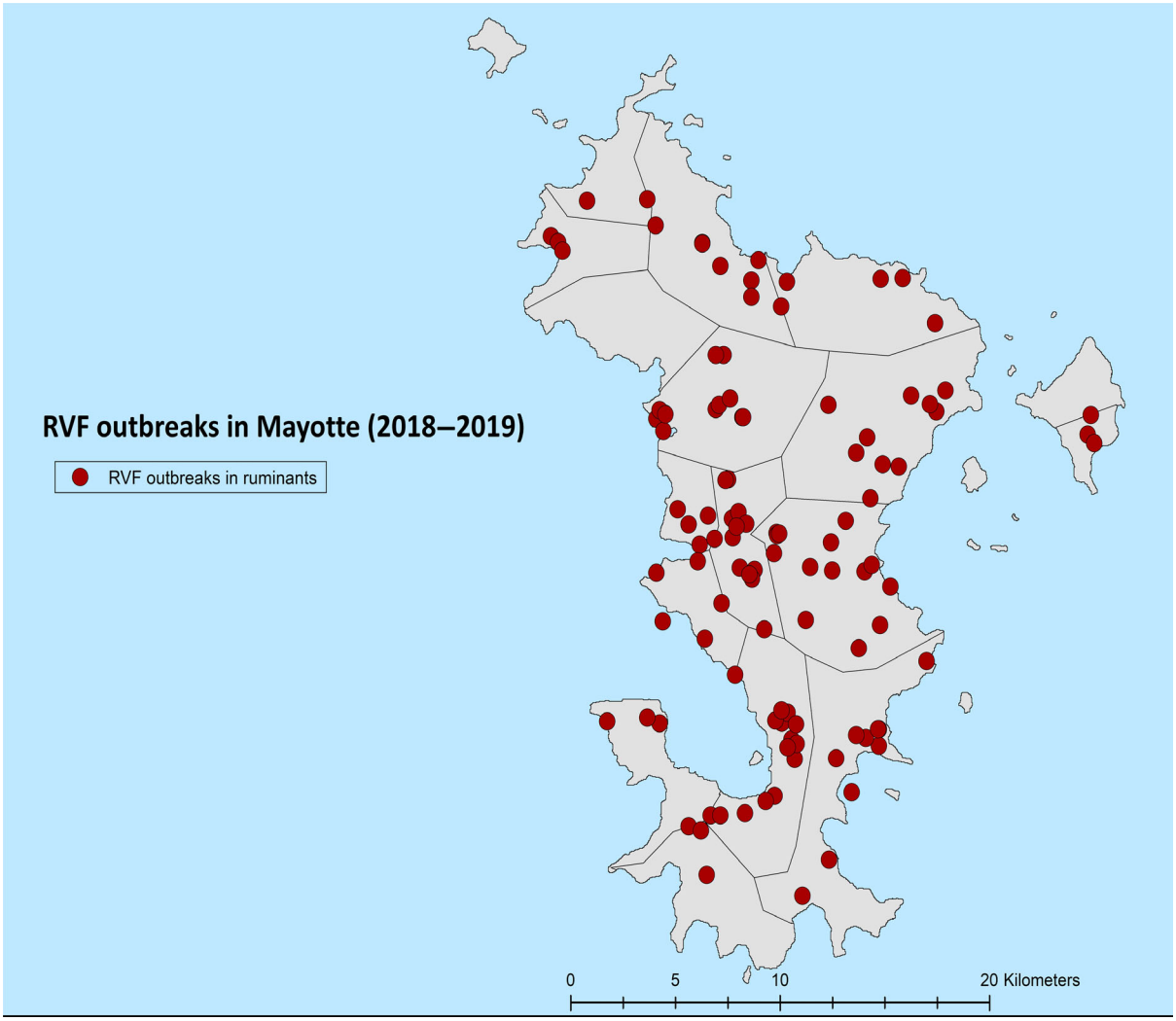

Figure 5: RVF reported outbreaks in Mayotte in 2018 and 2019 in ruminants (cattle, sheep, goats) as notified to the ADNS and provided by the French Veterinary Authorities

3.1.2.3. RVF seropositivity in countries officially RVF free

The results of some recently published studies, carried out in the countries surrounding the Mediterranean Basin, which never reported the disease either in humans or in animals, indicate the presence of a certain level of seropositivity in animals and in humans in some areas. These countries are: Turkey (Gur et al., 2017; Yilmaz et al., 2017), Tunisia (Bosworth et al., 2016), Iran (Fakour et al., 2017), Iraq (Muhsen, 2012; Saleh Aghaa and Rhaymah, 2013), Algeria (Nardo et al., 2014) and Western Sahara (El-Harrak et al., 2011; Nardo et al., 2014). In most of these studies, the sample size was limited, and the areas of study were limited. In many cases, details about the origin of animals tested are lacking, thus hampering a proper evaluation of the outcomes. Table 3 presents the results of the most recent studies published. In addition, the map in Figure 6 shows the geographical areas where seropositive results were observed.

Table 3: Publications indicating seropositivity in humans and/or animals in countries where RVF has never officially been reported either in animals or humans

Country	Sampling Period	Region, Province, Area	Species	No samples	Lab. Tests	Results	Publications
Iran	January to December 2016	Kurdistan Province	cattle	118	C-ELISA, IFA	1.7 % positive	Fakour et al. (2017)
			goats	28		negative	
			sheep	142		2.11 % positive	
Iraq	Unknown, before 2012	Basrah	sheep	1,215	ELISA (OIE)	8.88 % positive	Muhsen (2012)
	October 2012 to February 2013	Nineveh Province	sheep	184	C-ELISA	1.08 % positive	Saleh Aghaa and Rhaymah (2013)
			goats	184		4.89 % positive	
South West Algeria	March to April 2008	Refugee camps wilayas in Tindouf province and Dakhla Bir Lehlou Tifariti Mehaires	sheep	461	C-ELISA	1.12% positive IgG	Nardo et al. (2014)
North East Western Sahara			goats	463			
			camels	58			
Western Sahara	2009	Dakhla Smara– Laayoune	camels	100	C-ELISA, VN	15% positive	El-Harrak et al. (2011)
Morocco		Tata				negative	
Tunisia	summer 2014	Sousse Mahdia Sfax	humans	219	qRT-PCR	negative	Bosworth et al. (2016)
					indirect immunofluorescence testing kits	1.37 % IgG positive 6.84 % IgM positive	
Turkey	May 2013 to November 2016	Province of Istanbul	children	110	RT-PCR	negative	Yilmaz et al. (2017) (conference proceeding), presentation of the conference provided by Husein Yilmaz, and personal communication with Husein Yilmaz
					Indirect IgG ELISA	3.64 % positive	
					WB	6.3% positive	
		Provinces of Edirne, Kırklareli, Tekirdag in Marmara Region	cattle	200	RT-PCR	negative	
					Indirect IgG ELISA	4.5 % positive	
					WB	5.55 % positive	
			sheep	160	RT-PCR	negative	
					Indirect IgG ELISA	3.75 % positive	
					WB	5.6 % positive	
	2009–2012	Aydin Province	camels	72	C-ELISA	1.3 % positive	Gur et al. (2017)
	July to August 2005	Şanlıurfa Province	gazelles	82		negative	
	October 1999 to 2001	Afyon Province Amasya Province Samsun Province Ankara Province	water buffalos	352		9.94% positive	
		Sivas Province Tokat Province Konya Province Elazığ Province		58		negative	

Figure 6: Countries (Algeria, Iraq, Iran, Turkey, Tunisia and Western Sahara), where RVF seropositive results have been detected, with data available through publications or reports

On 15 January 2020, two RVF outbreaks have been notified to the OIE by the veterinary authority of Libya. The start of the event was reported as 12 December 2019. The two outbreaks are located in the south-eastern region of Al Kufrah, city of Aljouf, around 200 km and 300 km from the borders with Egypt and Sudan, respectively. In each outbreak (one with sheep and the other with sheep and goat animals), only one case has been declared. No deaths are reported. In the epidemiological comments section of the immediate notification, the following explanation is reported: 'As a part of surveillance carried out for Rift Valley fever in the whole country under the Food and Agriculture Organization project No.OSRO.LIB 801.CHA. around 150 samples from sheep and goat farms were collected by risk-based surveillance teams in Alkufra. Two samples from the Aljouf area gave a positive result'. Given this explanation, referring to serological positivity alone in the outbreaks, and the lack of major information about the origin of positive animals and the possible presence of clinical signs in the farms, it is difficult to provide any epidemiological evaluation about these two notified outbreaks. It is important to remember, however, that in the same period (end of 2019) a large RVF epidemic was notified in Sudan.

Key messages:

- RVF is historically present in sub-Saharan areas and in specific zones of the Arabian Peninsula, across the border between Saudi Arabia and Yemen.
- In the last two decades, more evidence has been obtained on the spread of RVFV to new African areas, not known as infected before, even in those areas considered not optimal for mosquito-borne diseases, like the pre-desertic areas of Sahel.
- Historically, major RVF epidemics have been cyclically observed in endemic areas, with long inter-epizootic periods (5–15 years) during which the virus was not detected in animal populations. In the last decade, RVF epidemics have been recorded more frequently and low-level enzootic RVFV circulation in livestock has been demonstrated in various areas.

- Outbreaks in a French overseas department and some seropositive cases detected in Turkey and Tunisia raised concern with the EU for a possible incursion into countries neighbouring the EU.
- Positive serological findings in Algeria, Western Sahara, Tunisia, Iraq, Iran, Turkey, which are countries considered officially free from RVF, must be carefully interpreted on the bases of the study designs and diagnostic tests used. However, the detection of serological positive individuals (animals or humans) in these countries must be seen as a potential risk of RVF spread out of its endemic geographical area.

3.1.3. Transmission and host range

3.1.3.1. Animal hosts

RVF affects domestic and wild ruminants and camels (FAO, 2003).

Camels

Dromedary camels (*Camelus dromedarius)* are susceptible to RVFV and infections have been recorded in most sub-Saharan African countries, with serological prevalence values ranging from 3.0 to 51.9 percent depending on the sampling period, strategy and location (Miguel et al., 2016). Widespread abortion waves associated with positive serologic test results were observed in dromedary populations during RVF outbreaks in Kenya and Egypt (Mroz et al 2017). During the 2010 outbreak in Mauritania, two clinical forms were observed in camels: (i) a peracute form with sudden death within 24 hours; and (ii) an acute form with fever, various systemic lesions and abortions. When haemorrhagic signs developed, death usually occurred within a few days (El Mamy *et al.*, 2011). However, mild forms and even a virus carrier state without clinical signs were also described. For instance, RVFV was isolated from blood samples from healthy, naturally infected dromedary camels in Egypt and Sudan (Eisa, 1984; Imam et al., 1979) while experimental infections did not induce clinical signs in non-pregnant dromedaries (Davies et al., 1985).

The potential role of dromedaries as amplifying hosts or virus spreaders remains unclear. Dromedaries may have brought the virus from north Sudan to south Egypt, where it caused the first Egyptian outbreak in 1977 (Eisa, 1984). A second study showed that RVFV was still circulating in dromedaries in Mauritania when the epidemic was officially declared over (El Mamy et al., 2014). In some areas, they may act as an amplifying host but do not seem to be essential to the epidemiological cycle of RVFV and its maintenance in all ecosystems. Viral circulation and/or large outbreaks have been reported in 'camel-free' countries such as Madagascar or countries in Central and Southern Africa, although the presence of various cycles in specific socio-ecosystems cannot be ruled out. From a zoonotic point of view, it is well known that transmission from cattle/small ruminants to humans occurs via direct contact with viraemic blood or infectious abortion products, but there is as yet no specific information about transmission from dromedary camels to humans (Miguel et al., 2016).

Wildlife

Although the exact epidemiological role of African buffaloes (*Syncerus caffer*) and other wild native or endemic ruminants for RVF is still not completely understood, they could contribute to the spread of the disease in eastern Africa as noted by several authors (Davies and Karstad, 1981; Anderson and Rowe, 1998; Evans et al., 2008; LaBeaud et al., 2011; Olive et al., 2012).

A recent experimental survey showed that white-tailed deer (*Odocoileus virginianus*), in North America, can transmit the virus through direct contact (n = 1) presumptively by the faecal–oral route (Wilson et al., 2018) : this result raises many questions about the potential role of wildlife in endemic areas, but also in Europe in case of introduction. There is Serological and sometimes virological evidence of an association between wild rodents and RVFV, but their involvement in the epidemiological cycle remains unclear (Olive et al., 2012).

Seventy-two lemurs were sampled and tested for RVFV during an interepidemic period in Mayotte by Metras et al. (2017) and showed no evidence of RVFV genome or antibodies in the samples (Metras et al., 2017).

Bats: several published studies of virus isolation, molecular evidence or seroconversion in bats have been published (Balkema-Buschmann et al., 2018; Kading et al., 2018; Nyakarahuka et al., 2018). However, whether or not bats serve as a reservoir of RVFV during interepidemic periods remains to be determined (Fagre and Kading, 2019).

3.1.3.2. Humans

Humans infected with RVFV mostly develop subclinical or relatively mild forms, showing only influenza-like clinical signs (CDC, 2013). A small proportion of infected people can develop more severe symptoms such as ocular disease, encephalitis and/or haemorrhagic fever, which can be fatal.

3.1.3.3. Vectors

RVFV has been isolated from field samples of more than 47 species of mosquitoes, including species in eight genera within the family Culicidae, where *Aedes* and *Culex* genera are considered to be the main vectors (EFSA, 2013; Linthicum et al., 2016; Lumley et al., 2017).

Transmission cycles are showed in Figure 7.

According to the previous EFSA Opinion on RVFV (EFSA, 2013), in general Rift Valley fever has been reported in four ecological systems: (i) dambo areas (African shallow wetlands), (ii) semi-arid areas, (iii) irrigated areas and (iv) temperate and mountainous areas. Typical endemic circulation of the virus in the dambo areas has been related to vertical transmission in the vector (adult to egg) and minimal amplification by vertebrates. Vertical transmission (VT) is hypothesised to allow the virus to persist during inter-epidemic and overwintering periods. However, up to now, it has been demonstrated only for two species (*Ae. mcintoshi* in Linthicum et al., 1985, originally reported as *Ae. lineatopennis*), and *Aedes vexans* (Mohamed et al., 2013) and no general evidence is available for other mosquito species or outbreaks elsewhere in Africa. Therefore, despite widely accepted, VT still remains generally undetected in most of the RVFV outbreaks recorded during the last 20 years and consequently, its role in maintaining the virus is uncertain (Lumley et al. 2017).

Epidemic transmission of RVFV has been related to heavy and prolonged rainfall mainly due to ENSO. In areas such as the dambo-type, it is known to occur every 5–15 years, where, according to the hypothesis of RVFV-infected *Aedes* eggs, these dormant eggs hatch and primary vectors *Aedes* adults transmit the virus to amplifying vertebrates (domestic ungulates) that trigger the epidemic cycle. High abundance of secondary vectors appears when stagnant floodwaters are colonised by *Culex* and *Mansonia* species that increase transmission to domestic animals and humans.

Similarly, outbreaks in semi-arid areas are characterised by the existence of temporary water points, and by permanent waterbodies that favour *Culex* populations breeding in irrigated areas, which, in temperate and mountainous areas, are also favoured by local vectors associated with specific cattle trade practices.

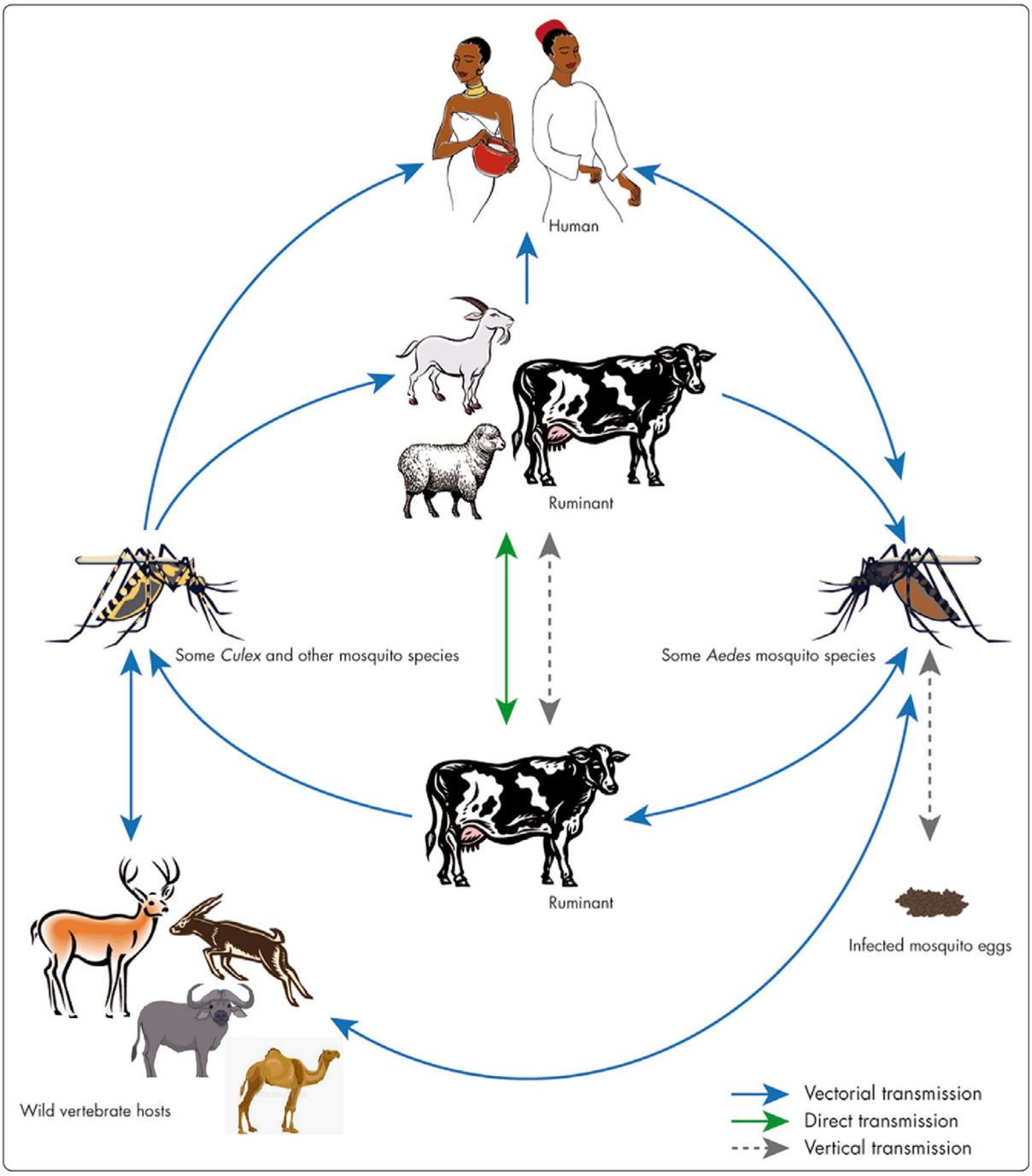

Figure 7: Cycle of transmission of the Rift Valley Fever virus. Vectors (mainly *Aedes* and *Culex* spp.) are able to transmit the virus to domestic and wild animals, as well as humans. Direct transmission is possible among animals and from animals to humans. Vertical transmission has been described in animals and vectors. The role of vertical transmission for maintaining the virus during inter-epizootic periods is still under discussion (modified from Balenghien et al., 2013)

Key messages:

- RVFV transmission is driven by several species of mosquitoes. Species belonging to *Aedes* and *Culex* genera are the most relevant for enzootic and epizootic cycles, respectively.
- Epizootic transmission is favoured by particular climatic conditions, such as heavy rains.
- Vertical transmission of the virus has been described in species of vectors, however, its role for explaining the survival of the virus during inter-epizootic periods remains unclear.

3.1.4. Laboratory diagnosis of RVF

There are several methods to diagnose acute RVFV infection in livestock and humans, either for virus detection or for antibody detection, but all must be carried out in laboratory settings.

3.1.4.1. Virus detection

The most appropriate matrix to isolate or detect RVFV is either whole blood or serum samples collected during the acute (febrile) stage of the disease or different organs collected post-mortem from fresh carcasses or aborted fetuses such as brain, liver and spleen. RVFV can also be detected in milk, although tests are not specifically designed for this material (unpublished results from COOPADEM, farmer association in Mayotte).

Isolation of RVFV can be obtained from (i) inoculation of suckling mice or (ii) inoculations of various susceptible mammalian or invertebrate cell cultures (OIE, 2018). A cytopathic effect is usually observed within 5 days from the day of inoculation, the presence of RVFV being confirmed by immunostaining. However, a faster and safer diagnosis can be achieved through molecular methods using real-time reverse transcriptase (RT)-polymerase chain reaction (PCR) to detect viral RNA (OIE, 2018) thus minimisng the handling of infectious viruses. Different highly sensitive molecular tests have been developed for RVFV including nested RT-PCR methods (Sall et al., 2002), quantitative real-time PCR (Garcia et al., 2001; Drosten et al., 2002; Bird et al., 2007; Wilson et al., 2013), multiplex PCR-based microarray assay (Venter et al., 2014), RT Loop-mediated isothermal amplification (RT-LAMP) (Le Roux et al., 2009) and recombinase polymerase amplification (RPA) (Euler et al., 2012). Molecular assays have also been used for the early detection of RVFV RNA in mosquito pools during surveillance activities (Jupp et al., 2002; LaBeaud et al., 2011). Point of care diagnostic tests have been developed in the past for the detection of RVF in mosquitoes (Turell et al., 2011; Wanja et al., 2011). More recently, a pen-side test for RVFV detection in the host compartment was developed through a lateral flow test (LFT) able to detect viraemic animals in the case of ongoing outbreaks which is likely to help to better manage the early diagnosis and control of RVF (Cetre-Sossah et al., 2019) with a level of DSe of 100% (CI 95%[90,1; 100]) (n = 35) and DSp of 98.8% (CI 95% [95.8; 99,7], n = 169). Lastly, other suitable tests for confirmation of clinical cases include histopathology followed by immunochemistry (Odendaal et al., 2014) and antigen detection ELISA (OIE, 2018).

3.1.4.2. Antibody detection

Serum samples collected from animals for serological testing need appropriate inactivation steps such as a combination of heat and chemical inactivation (van Vuren and Paweska, 2010). RVF antibodies can also be detected in milk, although tests are not specifically designed for this material (unpublished results from COOPADEM, farmer association in Mayotte).

Viral neutralisation tests (VNTs) and ELISA are suitable tests to detect the host induced immune response, immune status of individual pre- and post-vaccinated animals, identification of prevalence of infection and individual animal freedom from infection prior to movement (OIE, 2018).

The VNT remains the reference standard for detecting previous exposure to RVFV but while it is very specific, sensitive and useful to test samples from any host species of interest it is also costly, time consuming, and requires a high biosecurity laboratory capable of working safely with live RVFV.

One method of diagnosing acute or very recent infection is to use ELISA detecting IgM towards RVFV antigens (Williams et al., 2011) since IgG-based ELISA cannot distinguish between past and acute RVFV infections. Commercial assays kits are available as well as several in-house protocols have been published (van Vuren and Paweska, 2010; Fafetine et al., 2012); the performance of some of them has been compared in ring trials assays (Kortekaas et al., 2013). Sensitivity and specificity differ according to the antigens and protocols used (whole virus or recombinant proteins), and species investigated (domestic vs. wildlife species) (Paweska et al., 2005, 2008; Evans et al., 2008; Lubisi et al., 2019) (Table 4). An indirect ELISA based on the recombinant nucleocapsid protein of RVFV has been developed to differentiate between infected and clone 13-vaccinated animals (DIVA). In naturally infected animals, antibodies against both N and NSs would be detected, otherwise in individuals vaccinated with the clone 13 live-attenuated vaccines lacking NSs only an antibody response to the N protein would be observed (McElroy et al., 2009).

Alternative techniques such as the indirect immunofluorescence, agar gel immunodiffusion (AGID), radio-immunoassays and complement fixation are no longer used (OIE, 2018).

Table 4: Details of the commercially available (*) or in-house developed ELISA tests

Name (manufacturer)	Format	Antigen	Tested species	Validation data	References
ID Screen® Rift Valley Fever Competition Multi-species (ID Vet)*	Competitive	Np rec (E. coli)	Multiple species, including ruminants, camels, horses, dogs and others	Sp%: 100 (CI 95%: 99.58–100%), n = 920 (bovine, ovine, caprine, horses, dogs, cats, human) Se%: 100 (CI 95%: 91.24–100%), n = 40 (bovine from Djibouti and Mayotte collected in 2008; 18 tested in VN)	El Mamy et al. (2011) and Comtet et al. (2010)
ID Screen® Rift Valley Fever IgM Capture (ID Vet)*	IgM capture	Np rec	Domestic ruminants (Anti-bovine-ovine-caprine IgM antibody) Springbok (*Antidorcas marsupialis*)	Not provided by manufacturer	
RVF recN IgG Indirect ELISA (BDSL)**	Indirect	Np rec (E. coli)	Human and livestock		Jansen van Vuren et al. (2007)
RVF Inhibition ELISA (BDSL)**	Inhibition	RVFV inac	Human, domestic ruminants, buffalo, camel	Sp%: 99.47 (humans), 99.52 (cattle), 99.65 (goats), 99.29 (sheep), 99.51 (buffaloes), 100 (camels) Se%: 99.47 (humans), 100 (cattle), 99.56 (goats), 100 (sheep), 100 (buffalo), 100 (camel)	Paweska et al. (2005)
RVF IgM ELISA (BDSL)**	IgM capture	RVFV inac	Domestic ruminants	Sp%: 98.7(sheep) 99.7 (goats) 100 (cattle)	Paweska et al. (2003)
INgezim FVR Compact R.13 FVR.K3 (Ingenasa)*	Competitive	Np rec	Domestic ruminants	Sp%:99 (n. 1526 cattle, sheep, goats) (n.1014 deer, ibex, mouflons, fallow deer, alpacas and zebra) Se%:97 (31 sheep experimentally infected)	

Name (manufacturer)	Format	Antigen	Tested species	Validation data	References
INgezim FVR IgM R.13.FVR.K2-(Ingenasa)*	IgM capture	Np rec	Domestic ruminants	Sp%: 99.3 Se%: 95.7 1589 ovine, caprine and bovine sera (experimentally infected and vaccinated animals. The negative samples corresponded to different RVFV-free areas in Spain)	
	Indirect	Np rec (baculovirus)	Sheep, cattle	Sp%: 97 (sheep) to 100 (cattle) Se%: 100 (vs. PRNT in sheep and cattle experimentally infected)	Faburay et al. (2019)
	Indirect	Gn rec (E. coli)	Small ruminants	Sp%: 95.6 Se%: 94.6 (n. 1952 sheep and goat sera from Mozambique, Senegal, Uganda and Yemen)	Jäckel et al. (2013)
	Double Ag ELISA (IgM and IgG detection)	Refer to William (2011)	Cattle and sheep	Sp%: 100 Se%: 98.4 (412 sheep and 121 cattle)	Ellis et al. (2014)
	IgM capture	Np rec (E. coli)	Small ruminants and cattle	–	Williams et al. (2011)
	Competitive	Np rec (E. coli/ Mab)	Cattle and goat	Sp%: 99.7 Se%: 94.7 (n. 105 blood samples collected at intervals from experimental infection of 2 cattle and 5 goats)	Kim et al. (2012)
	Indirect	Np rec + NSs rec	Human, goats	–	McElroy et al. (2009)
	Indirect with IgG and IgM conjugates	Np rec (E. coli)	Sheep, goat, cattle	Sp%: 99.5–100 (goats), 100 (sheep), 98.3 (cattle) Se%: 99.4–100 (goats), 100 (sheep), 100 (cattle)	Fafetine et al. (2007)

*: Np rec, recombinant nucleocapsid protein; Gn rec, recombinant glycoprotein Gn; NSs rec, recombinant Non-structural proteins.
**: Not commercially available at the present.

3.1.4.3. Level of capability in the EU and Mediterranean

Diagnostic capability among EU Member countries and in the Mediterranean region has been assessed recently through European proficiency testing. A first proficiency testing involving six laboratories representing five EU countries (The Netherlands, France, Germany, Spain and UK) with some of them being national reference laboratories for RVF provided evidence of the proficiency of the participating laboratories (Kortekaas et al., 2013).

A broader proficiency test has been completed in 2014 including 11 laboratories from seven different countries within the REMESA network: three laboratories from Algeria, two from France, one from Mauritania, two from Morocco, one from Spain, one from Tunisia and one from Italy. Both RVFV genome and antibody detection were included in the external quality assessment in order to evaluate the diagnostic capacities and monitor the quality of the activities. CIRAD also performed a ring test in Mali and Senegal with satisfying results.

While six laboratories participated in both the viral genome detection by RT-PCR and the specific IgG and IgM antibodies detection trials, four laboratories participated exclusively in the antibody detection trial. Besides some limited misidentification of the samples, the two proficiency tests mentioned above provided evidence that most of the participating laboratories were capable to detect RVF antibodies and viral RNA thus recognising RVF infection in affected ruminants with the diagnostic methods currently available (Monaco et al., 2015). RVF diagnostic tests are in place in most of the other Mediterranean countries, nevertheless an evaluation of their performances should be encouraged through proficiency testing.

Key messages:

- Molecular assays to detect RVFV are available (gel-based and RT-PCR) and, more recently, a pen-side test for early detection of viraemic animals has been developed, and may become available;
- Serological tests to detect RVF antibodies and to distinguish early from past infection of RVF in domestic ruminants and camelids are available;
- In the EU, the diagnostic capability of the laboratories has been assessed and the level of performance considered adequate as well as in National Laboratories from Algeria, Mauritania, Morocco, Tunisia, Mali and Senegal;
- RVF diagnostic tests are in place in most of the other Mediterranean countries; nevertheless, an evaluation of their performances should be encouraged through inter-laboratory trials.

3.1.5. Possible geographical expansion and areas posing a risk for EU

In the previous EFSA Opinion on RVF (EFSA, 2013), the risk of introduction of RVFV through the movements of live animals and vectors into non-RVF-infected Middle East and Northern African (MENA[11]) countries (namely Morocco, Algeria, Tunisia, Libya, Jordan, Israel, the Palestinian Territories, Lebanon and Syria) was already assessed. In that Opinion, the Veterinary Services of the MENA countries reported that no official trade was in place with RVF-infected countries.

FAOSTAT database[12] accessed on September 2019, however, reported limited numbers of live ruminants and camels officially imported from RVF-infected countries by Algeria, Jordan, Lebanon and Morocco between 2009 and 2016 (Table 5).

Table 5: Number of animals (camels, cattle, sheep, goats) imported into MENA countries from RVF-infected countries between 2009 and 2016 (FAOSTAT, http://www.fao.org/faostat/en/#data)

Importing country	Exporting country					
	Egypt	Mauritania	Niger	Somalia	Sudan (former)	Total
Algeria	38		1,529			1,567
Jordan					57,437	57,437
Lebanon				3,521	975	4,496
Morocco		21				21

[11] https://it.wikipedia.org/wiki/MENA
[12] http://www.fao.org/faostat/en/#data

Although the numbers reported by FAO are modest, they can be considered as a proxy for unknown trade or not reported animals traded among these countries. It also highlights that data from Libya and Syria are not available probably due to the ongoing conflicts.

In relation to the possible introduction of RVFV through animal movements, the previous EFSA Opinion (EFSA, 2013) considered two main sources of infection:

- East source: South and North Sudan, Egypt, Somalia, Saudi Arabia, Yemen, Kenya, Tanzania,
- West source: Senegal, Gambia, Guinea Conakry, Cameroon, Sierra Leone, Mauritania, Mali, Niger and Chad.

When the main live animal trade routes are considered, however, for the sake of simplicity, three main pathways can be considered as potential ways to introduce RVFV into non-RVF-infected MENA countries (Bouslikhane, 2015):

- West Africa routes, including informal trade in live small ruminants and camels from the Sahel countries (especially Mauritania, Mali, Niger, Chad) to North Africa (Morocco, Algeria, Libya).
- East Africa routes characterised by the movement of live animals between countries in the Great Lakes region and along the Nile river. The latter, involving mainly South and North Sudan, Ethiopia, Djibouti and Egypt are of special importance for the possibility of RVFV to reach the Mediterranean coasts.
- Horn of Africa routes, involving the export of live animals from countries of the Region (mainly South and North Sudan, Ethiopia, Djibouti and Somalia) to the Gulf States and Middle East countries.

Other live animal trade routes may be recognised in northern Africa (Jenet et al., 2016), across the Sahara Desert, also involving animal exchanges between Maghreb countries (Bouguedour and Ripani, 2016), but the three main routes listed above can be considered as the most important for the potential introduction of RVFV into MENA countries (Figure 8).

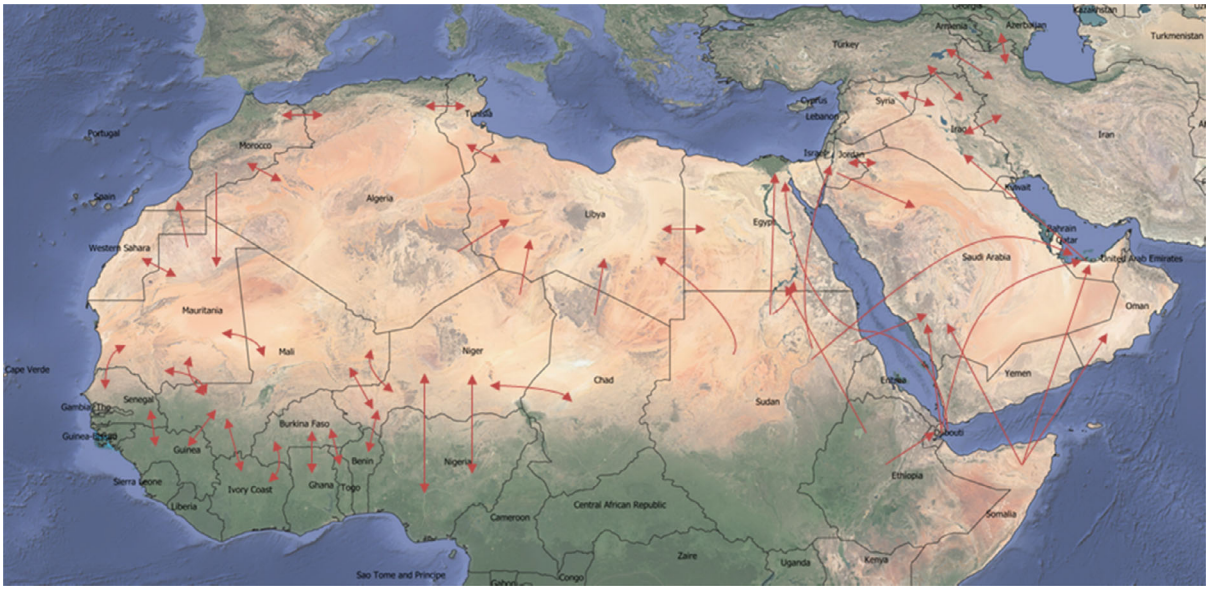

Figure 8: Principal movement pathways of live ruminants across North African and Middle East countries. Adapted from information reported by Bouslikhane (2015), (Di Nardo et al., 2011), Bouguedour and Ripani (2016), Jenet et al. (2016)

3.1.5.1. West Africa routes

In the Sahel and West Africa, transhuman pastoralism is one of the major livestock production systems, involving an estimated 70–90% of cattle and 30–40% of small ruminants (Touré et al., 2012). There is an agreement that this type of breeding preserves the environment and is viable, competitive and a provider of seasonal work (Bouslikhane, 2015). In the Sahel region, livestock mobility is essentially linked with pastoralism and it is driven by the need for access to natural resources and livestock markets. Mobility practices are driven by the geo-climatic, economical and sociocultural

conditions, including the search for water sources in the dry seasons, the need to move from areas affected by diseases or inter-ethnic conflicts and banditry (Bouslikhane, 2015).

The recent unrests following the so-called Arabian Spring, the instability in Libya and the increased insecurity in Sahel and Sahara regions followed by recrudescence of terrorism could be potential factors for altering the main livestock mobility routes, thus contributing to concentration of livestock in fewer areas and along fewer routes with unexpected spread of transboundary disease to new areas (EFSA Panel on Animal Health and Welfare, 2015).

In this Region, the main animal movement routes are from the Sahel to coastal countries: from Mali and Burkina Faso to supply Ivory Coast, Ghana, Togo and Benin ('central corridor'), from Chad, Niger, Sudan, Central African Republic, Mali and Burkina Faso to supply Cameroon, Nigeria, Benin and Togo, and from Mauritania and Mali to Ivory Coast, Senegal, Gambia and Guinea Bissau ('western route') (Gerber, 2010). However, unofficial animal movements between Sahel and Maghreb countries are well documented. Dromedary camels, probably arriving from Mauritania, were found serologically positive for RVF in southern provinces in Morocco (El-Harrak et al., 2011) and small ruminants with seroprevalence reaching 7% were found in the Sahrawi territories of Western Sahara, where animals are typically traded between Mauritania and Mali towards Algeria (Di Nardo, 2014). Animals originating from Chad and Sudan have been found in Libya, as well as sheep from Mali in the centre of Tunisia (Bouguedour and Ripani, 2016).

Concerning the risk of introduction of RVFV into Morocco, Algeria, Tunisia or Libya through these routes, the RVF epidemiological situation in West Africa is quite peculiar. Differently from East and South Africa, where classical 5–15 years inter-epizootic cycles are observed, western African countries have experienced in the last years an almost constant emergence of RVF outbreaks, and concurrent human cases (Arsevska et al., 2016): in 2010, 2012, 2013 and 2015 in Mauritania, 2013, 2014 and 2018 in Senegal, 2016 in Niger, 2017 in Mali and Nigeria, 2018 in Gambia and 2019 in Chad.

No evidence of possible RVFV introduction could be demonstrated in Libya (Mahmoud et al., 2018). However, these results must be carefully evaluated, especially regarding the representativeness of the sampled animals, given the current difficulties in accessing rural areas in Libya.

In Tunisia, during a study conducted in the summer of 2014, 18 human blood samples were positive for RVF. The serologically reactive samples were derived from febrile patients (n = 15, only IgM reactivity) and from afebrile farmers and abattoir workers (n = 3, only IgG reactivity) (Bosworth et al., 2016). These results indicate the occurrence of, at least, one undetected human outbreak of RVF in Tunisia. However, these laboratory outcomes must be carefully interpreted in the light of the performances of the diagnostic method used, the indirect immunofluorescence assay, which can be characterised by poor specificity in several instances. In addition, despite these results, to date, no RVF clinical cases were notified in Tunisia, neither in humans nor in animals.

3.1.5.2. East Africa routes

Four major RVF epidemics have been recorded in Egypt (1977, 1978, 1993 and 2003) (Kenawy et al., 2018), but a low level of RVFV circulation was observed during the inter-epidemic periods in various areas of the country along the Nile river (Mroz et al., 2017). Besides the local circulation of RVFV, the introduction of live animals from Sudan is considered as an important source of infection for Egypt (Napp et al., 2018).

A vaccination programme is in place in Egypt, where every year a great number of animals are vaccinated (General organization for Veterinary Services – Egypt) (Table 6) with an inactivated vaccine (Zagazig H501 strain) produced by the Egyptian Veterinary Serum and Vaccine Research Institute (VSVRI).[13]

Table 6: Vaccinated animals in Egypt in the 2016–2019 period

Year	Number of vaccinated animals					
	Cattle	Buffaloes	Sheep	Goats	Camels	Total
2016	2,923,648	1,552,856	642,711	54,452	216,884	5,390,551
2017	5,131,555	2,519,915	783,501	125,581	240,459	8,801,011
2018	3,840,535	1,891,061	477,761	84,438	218,916	6,512,711
2019*	4,186,385	2,213,411	421,311	78,463	131,169	7,030,739

*: Up to September.

[13] http://vsvri.com/Products/ProductsAnimal%201-4%20inactivated%20Rift%20Valley%20Fever%20Vaccine.html

In addition, the well-documented live animal cross-border movements with Libya may represent a further element of risk for RVF spread across northern Africa countries.

Recently, in October 2019, Sudan notified several human and animal RVF cases, causing great concern in neighbouring countries, such as Egypt and Ethiopia, and in the trading partners, like Saudi Arabia and Bahrain, which banned the import of live ruminants from Sudan.

3.1.5.3. Horn of Africa routes

The export of live animals from countries of the Horn of Africa towards the Arabian Peninsula is a well-accepted route. A substantial reduction was observed after year 2000 until 2007, when the Saudi Arabian authorities banned the introduction of live ruminants and camels from Somalia and Djibouti, in response to the introduction of RVFV in year 2000 through this route. Since 2007, the number of animals imported into the Arabic Peninsula from the Horn of Africa increased progressively, awareness has been raised about the risk of introduction of RVFV into Saudi Arabia. Last available statistics (FAOSTAT, http://www.fao.org/faostat/en/#data) for 2014 and 2015 show that around 7 and 7.8 million live domestic ruminants, respectively, were imported into the Kingdom of Saudi Arabia (Table 7) of which 98% were small ruminants (sheep and goats) and only around 100,000 dromedary camels. Of these animals, 61% originated from Sudan, whereas 35% were coming from Somalia.

Table 7: Number of animals (camels, cattle, sheep, goats) imported into Saudi Arabia, Yemen, Jordan and United Arab Emirates from countries of the Horn of Africa between 2003 and 2015 (FAOSTAT, http://www.fao.org/faostat/en/#data)

Year	Exporting countries						Total
	Djibouti	Egypt	Eritrea	Ethiopia	Somalia	Sudan	
2003	70,811	2,867	3,335		1,143,055	1,383,405	2,603,473
2004	199,777	2,895	6,110	206	762,533	1,930,122	2,901,643
2005	60,557	5,871	7,967	2,454	1,270,094	1,441,603	2,788,546
2006	82,350	400	11,779	1,160	1,260,143	1,440,851	2,796,683
2007	2,072,874	26,195	3,579	117,206	1,786,901	787,090	4,793,845
2008	77,655	92	475	39,377	1,344,108		1,461,707
2009	1,254,873		42,932		1,502,336	1,640,761	4,440,902
2010	265,843		20,544		2,018,253	1,823,583	4,128,223
2011	208,389			53,236	3,635,535	2,727,031	6,624,191
2012	479,006		443	34,789	3,945,769	3,668,696	8,128,703
2013	357,880			49,379	3,778,527	3,918,196	8,103,982
2014	388,651	24	7,330		2,765,597	4,110,817	7,272,419
2015	272,759		5,578	2,693	3,127,494	4,798,048	8,206,572
Total per country	**5,791,425**	**38,344**	**110,072**	**300,500**	**28,340,345**	**29,670,203**	**64,250,889**

The volume of live animals traded along this route reaches a peak during religious festivities. Two Muslim festivals must be considered: one (Lesser Bairam – Eid al-Fitr) falling at the end of Ramadan, the other (Greater Bairam – Eid al-Adha) 70 days later at the end of the Islamic year.

In the Islamic lunar calendar, Eid al-Adha falls on the 10th day of Dhu al-Hijjah and lasts for four days until the 13th day. In the international (Gregorian) calendar, the dates vary from year to year drifting approximately 11 days earlier each year, so it may fall in the vector season. During these Muslim celebrations, large numbers of sheep and goats are marketed for feasting and celebrations, particularly for the Greater Bairam (the sacrifice feast).

These trade routes from countries of the Horn of Africa towards the Arabian Peninsula were already identified as the cause of RVFV introduction into Saudi Arabia and Yemen in 2000, as well as an important way for the spread of other diseases, like foot and mouth disease (FMD) (Di Nardo et al., 2011).

To reduce the risk of introduction and spread of RVFV infection, the Middle East countries have adopted several control measures on live animals imported from countries not free from RVF. Considering the available information, some Middle East countries, such as Jordan or Saudi Arabia, request that animals be tested for the presence of antibodies against RVFV. In particular, Saudi Arabia, which is one of the larger importers of live animals from the Horn of Africa, requires that animals must

be kept in quarantine locations for not less than 21 days, where they are clinically inspected and serologically tested for various diseases, including RVF. Additional controls and quarantine periods are applied in the port of arrival.

Concerning the evidence of RVFV presence in Middle East, apart from the well-known and well-documented introduction of the virus into some regions across the borders between Saudi Arabia and Yemen (Saudi Arabia: Jizan, Asir and Al Quenfadah regions; Yemen: Wadi Mawr in El Zuhrah district of Hodeidah Governorate) (Kenawy et al., 2018), some papers had recently reported the possible evidence of RVF infection in other countries:

- In Iraq, serum samples were collected from 1,215 sheeps in five distinct regions of Basrah area (in the south of Iraq, close to Kuwait and Iran borders) and tested by c-ELISA for RVF, and 108 (8.9%) resulted positive. The serological prevalence was significantly higher in animals older than 3 years compared with other age groups (Muhsen, 2012). No information about the origin of animals or other details, useful to identify the possible time and place of exposure, were provided in the paper.
- In Turkey, serum samples collected from 72 dromedary camels during 2009–2012 and from 410 buffaloes from 1999 to 2001 were investigated for RVF using c-ELISA. One camel (1.4%) and 35 buffaloes (*Bubalus bubalis*) (8.5%) samples were positive for RVF-specific antibodies. The positive results were detected in four different provinces of Turkey: Amasya, Ankara, Samsun and Afyon (Gur et al., 2017). In addition, Yilmaz et al. (2017) detected antibodies against RVFV in 3.6%, 4.5% and 3.8% of tested children (n = 110), cattle (n = 200) and sheep (n = 160), respectively (see Section 3.1.2.3).
- In Iran, from January 2016 to December 2016, blood samples were collected from 288 ruminants (118 cattle, 142 sheep and 28 goats) of both sexes in the Kurdistan Province of western Iran. Clinical symptoms and history of abortions were recorded. The presence of RVFV-specific antibodies was investigated by c-ELISA and indirect immunofluorescence assay (IIFA). The results of both tests were positive for five (1.7%) out of a total of 288 animals, which included two cattle out of 118 (1.7%), and three sheep out of 142 (2.1%). The results of IIFA were correlated with the ELISA results. All animals were clinically normal.

It is very difficult to judge the relevance of these findings in the absence of official notification of RVF cases in animals or humans up until today in these countries. A more solid evaluation of the results of these studies could be done only with the availability of more detailed information about the origin and the history of the animals, and a clearer picture of the animal disease situation of the ruminants living around the locations where positive animals have been detected. In fact, given the epidemiology of the disease, single sporadic animal cases are unlikely to occur in a susceptible population, and may be explained only by animals being imported from infected areas or due to limitations of the diagnostic methods (false positives).

On the other hand, the results of these studies show the potential for RVFV (as well as other new emerging diseases) to move from Africa and the Middle East towards Europe, possibly facilitated by the presence of unofficial and uncontrolled animal movements (Di Nardo et al., 2011) and by the reduced levels of animal health controls in some territories due to conflicts and societal insecurity.

Key messages:

- The movement of live animals is the main risk factor for RVF spread from the African endemic areas.
- Several pathways of livestock movements between sub-Saharan and North African countries can be identified. It is reasonable to assume that a large part of these cross-border movements is currently not subjected to veterinary checks.
- The trade from the Horn of Africa towards the Arabian Peninsula and Middle East involves several million live animals each year, thus representing a risk of RVF introduction into the Middle East.

3.1.6. Control measures

3.1.6.1. Measures foreseen by the legislation

According to the Implementing Regulation (EU) 2019/1882, RVF belongs to the category A of the listed diseases that do not normally occur in the Union and for which immediate eradication measures must be taken as soon as it they are detected, as referred in Article 9(1)(a) of the Regulation (EU) 2016/429.

In Regulation (EU) 2016/429 of the European Parliament and of the Council of 9 March 2016 ('Animal Health Law') and in the Delegated Act supplementing Regulation (EU) 2016/429 of the European Parliament and of the Council, as regards animal health requirements for movements within the Union of terrestrial animals and hatching eggs,[14] control measures and activities have been provided at different stages of the disease: preparedness, suspicion and confirmation.

RVF is a category A disease so the final aim is eradication, not just control or to report cases. The controls in the Delegated Act will improve on 92/119 because better science about the pathogen and the epidemiology is available.

3.1.6.2. Vaccines

At present, no vaccines have been authorised for use in the EU by the European Medicine Agency (EMA, online). Their use for emergency vaccination should be ad hoc basis and authorised following the proper EU procedure.

Formalin inactivated and live-attenuated Rift Valley fever type of vaccines (LAV) represent the most developed and tested vaccines currently available for livestock immunisation. Both the inactivated and the live-attenuated vaccines (Smithburn and MP-12 strains) have been obtained from virulent RVFV isolates using conventional technologies, and represent the most sustainable strategy to mitigate the impact of RVF on livestock agriculture.

The live modified Smithburn vaccine can readily be produced in large quantities at low cost, and induces a durable immunity lasting at least 18 months following vaccination in sheep and cattle after a single inoculation (Coackley et al., 1967), although in a proportion of pregnant female animals, it may cause abortions or fetal teratology (Botros et al., 2006; Kamal, 2009). Genetic reassortment between RVF field strains and the Smithburn strain has been described in mammals (Grobbelaar et al., 2011) and mosquitoes (Turell et al., 2011).

In contrast to LAV vaccines, inactivated vaccines are described as safer, specifically for use in pregnant animals, though they are expensive to produce and require the administration of booster doses 3–4 weeks after initial vaccination to ensure adequate long-term protection (up to 38 weeks) (Lagerqvist et al., 2012).

Inactivated vaccines are normally used in non-endemic RVFV countries (CFSPH, online; O'Brien et al., 2016). Although both types of vaccines have contributed significantly to the control of RVF in endemic countries of Africa, the requirement of repeated immunisations (for inactivated vaccines) and risk of inducing teratogenic effects, abortion, and potential reassortment/reversion due to residual neuro-invasiveness and neurovirulence (for the LAV vaccines) highlight the need for a new generation of vaccines with a higher safety profile.

A critical advance over currently existing livestock vaccines would be the ability to discriminate naturally infected from vaccinated animals (DIVA). A DIVA approach (vaccine and accompanying diagnostic tests) is an essential requirement for vaccines to be used in both endemic and non-endemic countries allowing compliance with mandatory international trade restrictions during active RVF outbreaks.

Research focusing on RVF vaccine development has significantly increased in the past 10 years, with the vaccines having already been evaluated in rigorous safety and efficacy trials in relevant natural hosts, such as sheep and cattle. The availability of some of these new vaccines provides for the first time a realistic possibility to provide safe, effective and inexpensive vaccines for use in adult, pregnant and young animals.

RVF vaccines commercially available and vaccine candidates evaluated for their induced protection in different animal models are presented in Table 8 and Table 9.

Preventive mass vaccination is the most effective means to control RVF circulation when climatic, environmental and epidemiological evaluations suggest a high probability of RVF outbreaks.

[14] https://ec.europa.eu/transparency/regdoc/rep/3/2019/EN/C-2019-4058-F1-EN-MAIN-PART-1.PDF

Table 8: RVF vaccines and vaccine candidates evaluated for their induced protection in different animal models (adapted from Faburay et al., 2017). DIVA for differentiation between naturally infected and vaccinated animals. NHP for non-human primates

Type of vaccine	Host species involved in the protection evaluation studies	Commercially available	DIVA	References
1. Live-attenuated vaccines (LAV)				
1.1. Naturally attenuated				
Smithburn strain	Mice, sheep, goats, cattle	Yes	No	Smithburn (1949) and Botros et al. (2006)
MP-12	Mice, sheep, cattle, NHP, humans	No, but conditionally licensed to Zoetis Inc. for animal vaccination in the USA in 2013	No	Caplen et al., (1985), Saluzzo and Smith (1990), Vialat et al. (1997), Morrill and Peters (2011a, b) and Ikegami (2017)
Clone13/Clone13T (naturally NSs deleted 74HB59 strain of the Central African Republic)	Mice, sheep, goats, cattle and camels	Yes	Yes	Muller et al. (1995), von Teichman et al. (2011), Dungu et al. (2013), Daouam et al. (2015), Daouam et al. (2016), Makoschey et al. (2016) and Njenga et al. (2015)
1.2. Genetically modified attenuated				
R566	Sheep	No	Yes	Kortekaas et al. (2014)
Recombinant MP12 Δ/mutants	Mice, sheep, goats, cattle	No	Yes	(Ikegami et al. (2006), Morrill and Peters (2011a, b), Ly et al. (2017), Boumart et al. (2019) and Nyundo et al. (2019)
Recombinant MP12-Clone13	Mice	No	Yes	Lihoradova et al. (2012)
Recombinant ZH501 Δ/mutants	Mice, sheep, NHP	No	Yes	(Bird et al. (2008), Bird et al. (2011) and Smith et al. (2018)
Four segmented RVFV	Mice, sheep	No	Yes	Wichgers Schreur et al. (2017)
2. Virus vectored based				
Poxvirus	Mice, sheep, goats, NHP	No	Yes	Wallace et al. (2006), Pepin et al. (2010), Soi et al. (2010), Ayari-Fakhfakh et al. (2012), Ayari-Fakhfakh et al. (2018)
Newcastle disease virus	Mice, sheep, cattle	No	Yes	Kortekaas et al. (2010a) and Kortekaas et al. (2010b)
Adenovirus (CAdVax and ChAdOx1)	Mice, sheep, goats, cattle, camels	No	Yes	Holman et al. (2009), Warimwe et al. (2013) and Warimwe et al. (2016)
Modified vaccinia Ankara (MVA) virus	Mice	No	Yes	Papin et al. (2011), Lopez-Gil et al. (2013) and Busquets et al. (2014)
Equine herpervirus type1	Sheep	No	Yes	Said et al. (2017)
Alphavirus	Mice, sheep	No	Yes	Heise et al. (2009)
3. Non-replicable vaccines				
3.1. Inactivated type				
NDBR103 (Entebbe virus)	Mice, humans	No	No	Randall et al. (1962) and Eddy et al. (1981)

Type of vaccine	Host species involved in the protection evaluation studies	Commercially available	DIVA	References
TSI-GSD 200 (Entebbe virus)	Humans	No	No	Pittman et al. (1999)
Formalin inactivated (South African strain)	Sheep, cattle	Yes	No	Barnard et al (1977) and Harrington et al (1980)
Formalin inactivated (Menya/Sheep/258 strain)	Sheep, goats, cattle, buffaloes, camels	Yes	No	(Kamal (2011) and Fawzy and Helmy (2019)
BEI inactivated (strain ZH501)	Sheep, goats, cattle	Yes	No	
3.2. DNA and subunit based				
Recombinant Gn protein	Mice, sheep, cattle	No		Schmaljohn et al. (1989), Wallace et al. (2006), De Boer et al. (2010), Faburay et al. (2016)
DNA	Mice	No		(Spik et al. (2006), Wallace et al. (2006) and Lagerqvist et al. (2009)
Sub-unit vaccine (Gn-e/Gn-Gc)	Mice, sheep	No	Yes	Schmaljohn et al. (1989), De Boer et al. (2010), Kortekaas et al. (2012) and (Chrun et al. (2019)
3.3. Virus Like Particle (VLP) based				
VLPs	Mice	No	Yes	(Liu et al. (2008), Naslund et al. (2009), De Boer et al. (2010), Mandell et al. (2010) and Mbewana et al. (2019)
4. Single cycle replicable based vaccines				
4.1. RVFV replicon particles (RRP) or non-spreading RVFV (NSR)	Mice, sheep	No	No	Kortekaas et al. (2011), Dodd et al. (2012) and Oreshkova et al. (2013)
4.2. MP-12-based single-cycle replicable particle	Mice	No	No	Murakami et al. (2016) and Terasaki et al. (2016)

Table 9: Details of the RVF vaccines commercially available and countries of licence and/or use

Commercial Vaccine (viral strain)	Manufacturer	Animal species	Country of licence or use (u)	Notes
RIFTVAX TM (Smithburn strain)	Kenya Veterinary Vaccine Producing Institute (Kenya)	cattle, sheep and goats	Kenya	
Rift Valley Fever (Smithburn strain)*	Veterinary Serum and Vaccine Research Institute (Egypt)	cattle, sheep and goats	Egypt	Smithburn strain imported from South Africa
Rift Valley formalin inactivated (Menya/ Sheep/258 strain)	VACSERA (Egypt)	cattle, sheep and goats	Egypt	
Rift Valley BEI inactivated (ZH501 strain)	Veterinary Serum and Vaccine Research Institute (Egypt)	cattle, sheep and goats	Egypt	

Commercial Vaccine (viral strain)	Manufacturer	Animal species	Country of licence or use (u)	Notes
Rift Valley Fever formalin inactivated (SA field strain)	Ondersterpoort Biological products (South Africa)	cattle, sheep and goats	South Africa, Namibia, Tanzania (u), Botswana (u)	
Rift Valley Fever live attenuated (Smithburn strain)	Ondersterpoort Biological products (South Africa)	cattle, sheep and goats	South Africa, Namibia, Egypt (u), Kenia (u), Zimbabwe (u), Tanzania (u), Sudan (u), Saudi Arabia (u), DRC (u)	From serial passages of the Entebbe strain
RVF Clone13 live attenuated (clone 13)	Ondersterpoort Biological products (South Africa)	cattle, sheep and goats	South Africa, Namibia, Botswana, Zambia, Mozambique, Zimbabwe (u), Kenya (u), Senegal (u)	Clone of 74HB59 strain from a human patient in the Central African Republic
Riftovax-LR live attenuated (clone 13T)	MCI Sante Animale (Morocco)	cattle and camels	Morocco, Senegal (u), Mali (u)	Thermostable Clone 13 vaccine
Riftovax-SR live attenuated (clone 13T)	MCI Santé Animale (Morocco)	sheep and goats	Morocco, Senegal (u), Mali (u)	Thermostable Clone 13 vaccine

*: Not produced at the present.

Key messages:

- No vaccines against RVF have been so far authorised for use in the EU. Their use for emergency vaccination should be on an ad hoc basis and authorised following the proper EU procedure.
- Both live-attenuated and inactivated vaccines are commercially available for RVF and have contributed significantly to the control of RVF in endemic countries. However, they require repeated vaccinations (inactivated vaccines) and retain the risk of teratogenic effects, abortion and potential reassortment/reversion to virulence (live attenuated).
- Several novel candidate vaccines are in the final stages of validation and, among them, most allow to discriminate naturally infected from vaccinated animals (DIVA).
- Preventive mass vaccination is the most effective means to control RVF circulation when climatic, environmental and epidemiological evaluations suggest a high probability of RVF outbreaks. However, the use of vaccines should be carefully evaluated once the virus transmission has already been detected in the area since it may intensify transmission among herds through needle propagation of the virus.

3.1.6.3. Vector control

Up until now, there are no records on the use of vector control methods for decreasing transmission of RVFV. Theoretically, RVFV epidemics can be controlled by applying larvicides and/or adulticides during specific moments of the cycle of transmission. In Africa, it is suggested that larvicide treatments should be conducted after heavy rains in the flooded dambo areas before the occurrence of primary vectors (*Aedes* spp) and/or secondary vectors (mainly *Culex* spp.). Use of adulticides is recommended after the period of breeding of secondary vectors in stagnant waters, since those vectors would increase transmission due to high density population in the area (Linthicum et al., 2016). The large number of mosquito species that transmit RVFV in Africa and the distribution and extension of breeding sites, particularly after heavy rains, makes it very difficult to successfully apply any method of control on a large scale to prevent transmission of the virus (Balenghien et al., 2013). In addition, while control by vaccination is still the main tool for the disease and vector controls, being desirable from a One Health perspective, it is still widely under-implemented (Fawzy and Helmy, 2019).

Mosquito control methods are well developed in the EU, and, differently from other vectors such as *Culicoides* spp., breeding sites can be controlled either by physical or chemical/biological methods (i.e. *Bacillus thuringiensis*). Examples of mosquito control can be found for species causing nuisance in

cities and periurban areas (e.g. *Ae. albopictus*), as well as for mosquitoes present in wetlands and coastal environments (e.g. *Ae. vexans* and *Ae. caspius*). The control of vectors in urban and periurban areas is mainly related to the control of transmission to humans, while methods used for controlling in wetlands and salt marsh environments can be related to both humans and animals (domestic and wild). In the EU urban areas, mosquitoes are mainly controlled by community education, source removal to avoid oviposition and larval development, biological insecticides such as *B. thuringiensis israelensis* (*Bti*) and *Lysinibacillus sphaericus (Ls)*, Insect Growth Regulators (IGR diflubenzuron, pyriproxyfen) in some MS, as well as surface films that impede larval breathing. Adulticides (e.g. outdoor spraying of pyrethroids) are used in adult mosquito resting areas in case of local transmission of imported arbovirosis such as dengue, Zika and chikungunya, or after natural catastrophes such as floods, which increase breeding sites. All these methods can be applied in the EU in case RVFV is introduced and transmitted by local vector species (e.g. *Cx. pipiens*), but there is no information about the effect of those control measures in the rate of transmission of the virus.

There are previous experiences in Europe on vector control to decrease disease transmission. Vectors of malaria were controlled during the 50s mainly because of environmental water management and the use of DDT. Sanitation is still one of the cornerstones of mosquito control in Europe; however, the use of DDT is forbidden and even the wide use of other adulticides is very limited due to environmental concerns. Similar to RVFV, other viruses such as West Nile (WNV) are also mainly transmitted by *Cx. pipiens* s.l. Outbreaks of WNV are detected each year in the EU (Haussig et al., 2018) and despite vector control measures being applied, there is no information on their impact on virus transmission. Main preventive measures are based on source reduction strategies, while ground insecticide treatments are recommended just in the case of outbreaks (Bellini et al., 2014).

Currently, mosquito species (e.g. *Ae. vexans*, *Ae. caspius, Cx. pipiens*) breeding in large freshwater flooding areas, salt marshes and irrigation channels are regularly controlled in the EU, mostly because of them being a nuisance, by the use of *Bti* and *Ls (Becker and Zgomba, 2007)*.

Additional methods for controlling adults are available, such as the Sterile Insect Technique (SIT) that is currently in use in Italy for the control of the invasive Asian tiger mosquito (*Ae. albopictus*) (Bellini et al., 2013). This method is area wide based and in certain conditions, and, theoretically, is able to reduce the mosquito population, having an impact on the transmission of the pathogen. However, some of the main constraints of this technique is the cost and that it is species specific, which means that SIT should be developed for each of the species related to the transmission of RVFV. If RVFV is introduced into Europe, according to results on vector competence in laboratory trials, it is likely that several species of mosquitoes will be able to transmit it (e.g. *Cx. pipiens*, *Ae. vexans* and *Ae. albopictus*) (Ducheyne et al., 2013; Brustolin et al., 2017).

Similarly, to other vector-borne diseases, such as bluetongue, blood-feeding insect repellents may play a role in protecting animals from vector bites. In the EU, mosquito repellents are mainly used for high value animals (e.g. horses) (Chapman et al., 2018) and little data are available about its efficacy in livestock animals that could be widely affected by RVFV.

Key messages:

- There is no information about the use of vector control strategies to decrease transmission of RVFV in Africa. Field implementation appears to be challenging due to the large number of vector mosquito species and the wide extension of breeding sites.
- Mosquito control tools are well developed in the EU for urban, periurban and natural environments, mainly by using source reduction and biological origin insecticides (e.g. *Bacillus thuringiensis israelensis*).
- There is no information about the efficacy of the current mosquito control tools for decreasing arboviruses present in the EU (e.g. West Nile virus) that are transmitted by the same species that transmit RVFV in Africa.

3.2. Risk of introduction of RVF into EU

3.2.1. Possible pathways for introduction into EU

RVFV can be introduced into a new region by several pathways (EFSA, 2005, 2013). The role of infected animals, infected vectors, contaminated products and infected humans is reviewed in the following sections.

3.2.1.1. Animals

Potential pathways for RVF introduction into the EU are the trade of livestock or the uncontrolled movement of livestock and/or captive susceptible animals (zoo animals). RVF virus replicates to very high titres in many species (e.g. viraemia of 10^4 to 10^9 PFU/ml for several days). The viraemia can last up to 4–5 days in sheep (Weingartl et al., 2014; Faburay et al., 2016) and 1–7 days in cattle (McIntosh et al., 1973).

Livestock importation

The movement of live animals into the Union is regulated by several pieces of legislation (which will be brought together under the AHL, 2016/429), which means there are very few countries outside the EU which are approved for the import of live animals, in particular ungulates (ruminants and camelids). The list of these countries is in Annex I of 206/2010/EU. There are no countries approved which are endemic for RVF. Imports of non-livestock ungulates between confined establishments may be agreed by an EU MS provided a risk assessment is undertaken on the establishment of origin and the animals are moved with a certificate and with the health attestation and pre-movement testing and quarantine according to 780/2013/EU.

According to the EUROSTAT database, there is no movement of live bovines or live sheep and goats from extra-EU countries that are affected or endemic of RVF towards the EU. Such movements, in fact, are forbidden by the EU legislation.[15] In the UN COMTRADE database,[16] some figures are reported about the importation of very few cattle (2–4 individuals) from Botswana towards Germany and France between 2015 and 2018, but these are probably zoo animals normally subjected to strict checks. In the same database, no trade is recorded for other mammals like primates, rabbits, hares, camels.

Uncontrolled movements of animals

In the EU, despite several directives and regulations pertaining to the import of animals and products of animal origin and veterinary controls on importation, uncontrolled movements of animals and animal products still occur worldwide and may favour the spread of transboundary diseases. The illegal transport of live animals is linked to several drivers at the socio-economical (poverty, urbanisation, demographic change), political (unrests) or geographical (e.g. droughts, remote areas) levels (EFSA Panel on Animal Health and Welfare, 2015). Nevertheless, given the affected countries in Africa without geographical contiguity to MSs, the uncontrolled transboundary movement of live animals from those countries to EU can be considered very difficult if not impossible.

3.2.1.2. Animal products

Import of fresh or frozen meat from ungulates from third countries is also regulated under 206/2010 (Annex II) there are only a few sub-Saharan countries authorised; the meat must be deboned and matured to a pH which would destroy viruses including RVF. Milk products import are controlled by Regulation (EC) 605/2010 where the list of authorised third countries is indicated, there are only a few African/Middle East third countries approved, and then, only for heat-treated products.

Rift Valley fever virus can be transmitted to humans also through direct contact with contaminated bodily fluids and tissues and fresh animal products such as milk or meat. The degree of exposure to RVFV-infected bodily fluids and tissues varies by types of behaviours engaged for occupational tasks. While previous studies have included exposure to milk, their primary focus on livestock exposures has been on animal handling, breeding and slaughter. Data from multiple field surveys in Kenya were analysed and revealed that exposure to raw milk may contribute to a significant number of cases of RVFV, especially during outbreaks and in endemic areas, and that some animal species may be associated with a higher risk for RVFV exposure (Grossi-Soyster et al., 2019).

The above is linked to fresh products. Because RVFV is highly sensitive to low pH and thus quickly inactivated in maturing meat or dairy products, this pathway of possible introduction of RVFV into EU from infected areas has not been considered in this assessment, also because of the limited amount of trade of these commodities from RVF-infected areas. Other biological material such as serum, plasma

[15] Council Directive 91/496 on veterinary checks on animals entering the EU from third countries; Council Directive 97/78/EC on organisation of veterinary checks on products entering EU from third countries; Commission Decision 2003/623 about development of an integrated computerised veterinary system known as Traces; Commission Regulation 136/2004 on the procedures for veterinary checks at EU BIPs on products imported from third countries; Commission Decision 2007/275 on lists of animals and products to be subject to controls at Border Inspection Posts (BIPs); Commission Regulation 206/2009 on the introduction into the Community of personal consignments of products of animal origin.

[16] https://comtrade.un.org/

or vaccines may represent a source of infection only if moved intentionally such as in bioterrorism acts, but the chance of this is considered to be of less importance compared to other pathways.

3.2.1.3. Vectors

Due to its size and biology, the different biological stages of mosquitoes (egg, larva, pupa and adult) can be transported over long distances by different means of transportation, such as airplanes, boats and road vehicles (Lounibos, 2002). In addition, wind streams are able to transport mosquito adults in the so-called 'aerial plankton'. During the last 50 years, air, sea and road transportation have increased significantly, increasing the introduction of arboviruses and in some cases, their vectors (Tatem et al., 2006; Tatem et al., 2012).

Some species of mosquitoes, which are potential vectors for RVFV, such as *Ae. aegypti*, *Ae. albopictus* and *Ae. japonicus*, share a similar ecology adaptation to oviposit in man-made water containers and feed on human blood (Calzolari, 2016). Therefore, they have higher probability of being passively transported by human means compared to other species that breed in non-human related habitats and have animals as preferred host (e.g. *Culex* species). Passive transportation and introduction in new areas has been widely recognised for *Ae. aegypti*, *Ae. albopictus* (Medlock et al., 2012; Collantes et al., 2015) and *Ae. japonicus* (Kaufman and Fonseca, 2014).

The biology of some of the species also favours the transportation. For example, eggs of some strains of *Ae. albopictus* are able to survive prolonged periods without water showing a true biological diapause (Tran et al., 2013). This feature makes this species an excellent candidate for being transported by different commodities such as used tyres, as well as 'lucky bamboo' (*Dracaena sanderiana*; Dracaenaceae) and Bromeliaceae plants (Schaffner, 2003; Scholte et al., 2008; Scholte et al., 2012). In fact, second-hand tyre trade has been identified as the major source of *Aedes* invasive mosquito species introduction in Europe and it is well documented in European countries such as France since 1999 (Roche et al., 2015). On the other hand, *Culex* species lack drought resistant eggs, since oviposition is conducted on water layer and not in the walls of small containers, such as is the case of *Aedes* species. Consequently, there is relatively low risk of transport of *Culex* species by means of transport of commodities (i.e. tyres) compared to the *Aedes* ones. This is relevant for the RVFV transmission, since *Aedes* species are considered primary vectors in Africa, and they are able to maintain the virus in drought resistant eggs that would emerge as infected females starting transmission in nearby animals. Additionally, *Culex* species are considered as secondary vectors, in combination with some *Anopheles* and *Mansonia* species, that contribute to increase transmission of RVFV (Sang et al., 2017).

According to the assessment performed by the Vectornet consortium (Wint et al., 2020), of the 39 identified potential vectors of RVFV, five were ranked highest based on their potential role as vector, and their behavioural and ecological traits influencing the risk of transportation. These species were *Anopheles pharoensis, Aedes aegypti, Mansonia uniformis, Aedes mcintoshi* and *Culex quinquefasciatus.* The African countries ranked according to the presence of the 10 highest potential RVFV mosquito vectors are South Africa, Kenya, Mozambique, Nigeria, Sudan and Uganda (section 2.2.2.1). These countries are also heavily connected to the EU Member States and contributed for 72% of the direct flights from the at-risk countries to the EU Member States in 2018.

From the five species of mosquitoes selected with the highest rank to be transported from RVFV-affected countries in Africa, only *Ae. aegypti* (only in Madeira island and sporadic detection at Schiphol International airport, the Netherlands) is present in the EU.

The list of RVFV potential vectors present at the EU can be checked at the EFSA's vector-borne disease map journals.[17]

Passive transportation by air, sea and road

Aircraft introduction

Adult mosquitoes have been detected in air cabins and gangways (Eritja et al., 2000; Karch et al., 2001; Bataille et al., 2009). The number of mosquitoes found inside aircrafts vary from 2.25 WNV-infected mosquitoes/year on 74 flights from USA to Barbados (0.03 mosquitoes/aircraft) (Douglas et al., 2007); 50 mosquitoes on 89863 aircraft in a 9-year survey (0.0005 mosquitoes/aircraft) (Le Maitre and Chadee, 1983) to 686 mosquitoes on 307 aircrafts (2.2 mosquitoes/aircraft) (Russell et al., 1984). Haseyama et al. (2007) identified 26 mosquitoes on 2161 flights (≅1 mosquito each 100

[17] https://efsa.maps.arcgis.com/apps/MapJournal/index.html?appid = 5caa3b6f07684ce881301ea2326bc811

flights) arriving to Narita Airport in Japan from 2001 to 2005. This study was also used by Brown et al. (2012) to estimate by modelling, the number of WNV positive mosquitoes entering to UK via flights from USA. Results from the model indicated that there was a very high risk of importation of WNV-infected mosquito from the USA to UK. However, the authors also recognised that there is a high level of uncertainty when estimating the number of mosquitoes per aircraft. In the Netherlands, Scholte et al. (2014) found 14 mosquitoes in 10 flights from a total of 38 inspected flights with origin from different locations. All mosquito interceptions were recorded in flights arriving from Africa. The study conducted by Mier-y-Teran-Romero et al. (2017) estimated that approximately an average of 0.91 mosquitoes (95%CI: 0.00009–5.3) were found per aircraft after analysing 17 studies of the presence of mosquitoes on 559,579 aircraft from 1931 to 1999. It was concluded that malaria was 1000 times and dengue 200 times more likely to be introduced by infected travellers when compared to the introduction via infected mosquitoes. Similarly, the overall probability of introduction of RFVF vectors through human transportation was considered of minor importance in comparison with the probability of movement of RVFV-infected animals in a previous EFSA opinion (EFSA, 2013). The low number of mosquitoes transported by air was also confirmed by a recent detailed report on the mosquito interception at airports of New Zealand from 2001 to 2018, showing that only 83 mosquitoes were intercepted (5 mosquitoes/year), including 15 adults of *Ae. aegypti* and one adult of *Ae. albopictus* (Ammar et al., 2019). In general, mosquitoes transported in airplanes are considered less probable to establish due to the low number of adults transported. However, despite its low number, for some diseases such as malaria and dengue, one single infected female may have important epidemiological relevance because of the cases detected in the surroundings of airports in disease-free countries (Gratz et al., 2000; Whelan et al., 2012). There is a probability that RVFV vectors (i.e. *Culex* species) may also be introduced by plane and therefore to transmit the virus in the surroundings of airports; however, this probability should be considered very low according to models obtained for human diseases (Mier-y-Teran-Romero et al., 2017). This also depends on the number of flights connecting RVF-infected countries and Europe, since the number of vectors can be scaled up (Figure 9).

Disinsection of aircrafts is recommended by WHO (WHO, 2016a), in particular to prevent the spread of human diseases (yellow fever, dengue and malaria, etc…) and was updated after the outbreaks of the Zika virus in 2016 (WHO, 2016b). Disinsection consists of insecticide treatment of aircraft interiors and holds, and the current procedures (i.e. pre-flight; blocks away; top-of-descent; and residual treatment) are considered efficacious for mosquito elimination from aircrafts (Russell and Paton, 1989) (WHO, 2016b). However, up to now there is no evidence of the efficacy of these measures in preventing VBD transmission compared to the high volume of infected humans that are transported on a regular basis (Grout, 2015; Mier-y-Teran-Romero et al., 2017). There is also a lack of information on the efficacy of vector control procedures to prevent the introduction of VB animal diseases by infected mosquitoes. Due to the importance of human diseases such as malaria, dengue, chikungunya and yellow fever, a vector-borne disease airline importation risk tool (Vector-borne Disease Airport Importation Risk Tool, http://vbd-air.com/) has been developed for estimating the risk of disease transmission due to aircraft transportation considering global vector and disease distribution as well climate and seasonality (Huang et al., 2012). To our knowledge, there is not an equivalent tool in the case of vector-borne animal diseases.

According to the assessment conducted by Vectornet (Van Bortel et al., 2020), the probability of importation of vectors through air was driven by the number of direct flights from at-risk countries to the respective EU Member State. The probability was around 0.5 (from 0.579 to 0.452) for the Netherlands, France, Germany and Italy, followed by Spain, Poland, Belgium and Austria with a probability of 0.287, 0.204, 0.202 and 0.163, respectively.

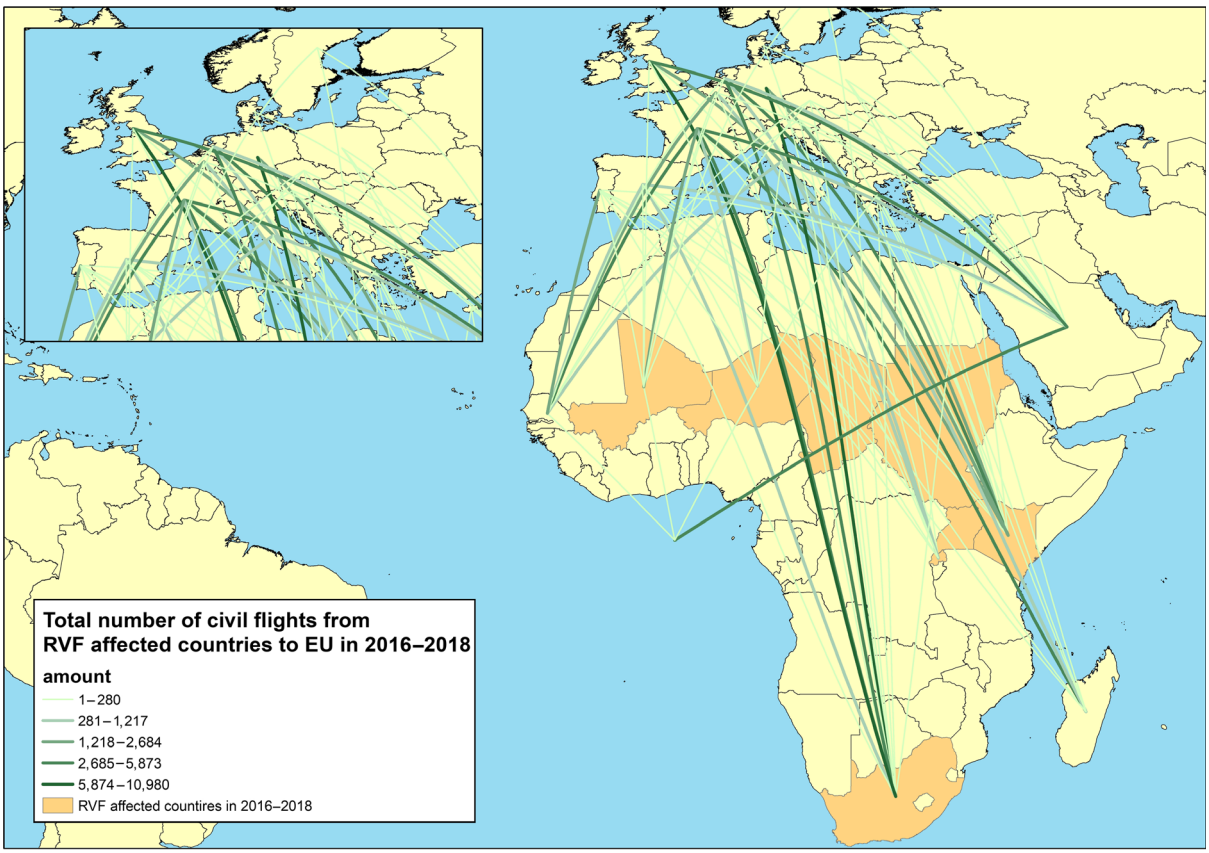

Figure 9: Number of outbound civil flights in 2016–2018 from countries that have reported RVF outbreaks in the same period

Sea transport introduction

Introduction and worldwide expansion of invasive Aedine species such as *Ae. albopictus* has been related to ports with high traffic volumes that increase the risk of invasion from areas that share similar eco-climate conditions (Grout, 2015). Sea routes seem to play a major role in long distance dispersion of *Aedes* invasive species compared to air traffic volume either by transporting eggs in tyres and/or adults in plants. The same can be said for high-risk sea traffic routes identified for *Anopheles* species in Africa (Tatem et al., 2006).

Introduction of *Ae. albopictus* by sea transport has been recognised in Italy (Dalla Pozza et al., 1994), France (Roche et al., 2015) and the Netherlands (Scholte et al., 2008). In general, there is limited information about the number of mosquitoes detected in sea transport in comparison with air transport. Dalla Pozza et al. (1994) found 380 larvae in 10 airplane tyres transported from USA, while Scholte et al. (2008) found 569 adults in 724 shipments (41 million plants) of 'lucky bamboo' importations to the Netherlands from China during 2006 and 2007. In New Zealand, 161 mosquito interceptions were recorded from 2001 to 2018 (9.5 mosquitoes/year). From those, the majority were *Ae. albopictus*, *Ae. aegypti* and *Cx. quinquefasciatus* (Ammar et al., 2019).

Road transport introduction

There is evidence that adult mosquitoes can be locally dispersed by road vehicles. A work conducted in the Barcelona area estimated that between 3 and 16 of every 1000 cars were carrying adult tiger mosquitoes during the summer period (Eritja et al., 2017). There is also evidence of *Ae. albopictus* eggs detected in resting areas along highways far away from the established area, which is consistent with a 'leapfrog' model of dispersion of adults inside vehicles (Roche et al., 2015; Tavecchia et al., 2017). Similarly, Egizi et al. (2016) also showed the role of humans in the transportation along roads for the spread of *Ae. japonicus* in several states of the USA.

Wind introduction

Verdonschot and Besse-Lototskaya (2014) reviewed active and passive movement of mosquitoes. They provide a summary of the findings in published literature for long distance windborne dispersal for different species of mosquitoes. The range of windborne transfer was from 97 km for *Ae. vigilax* to 850 km for *Cx. pipiens pipiens.* For other potential RVFV vectors such as *An. Pharoensis, Cx. tritaeniorhynchus* and *Ae. Vexans,* they reported windborne transportation over 280, 500 and 740 km, respectively.

There is circumstantial evidence of windborne transportation of mosquitoes of at least 500 km from Sudan that resulted in epidemics of RVFV in 1977 in Egypt (Sellers et al., 1982; Pedgley, 1983). There is also evidence of mosquito transportation by prevailing winds, such as bovine ephemeral fever outbreaks in Israel in 1990, 1999 and 2004, with transport of mosquitoes 180 km from Egypt to the Jordan Valley (Yeruham et al., 2010).

Active dispersal

In general, it is considered that active flying of mosquitoes would transport them to maximum distances between 50 m and 50 km, with the average flight range being between 25 m and 6 km (Verdonschot and Besse-Lototskaya, 2014). Linthicum et al. (1985) studied the active dispersal of potential RVF vectors (e.g. *Ae. mcintoshi*, originally reported as *Ae. lineatopennis*) in Kenya. In general, they found that the mean dispersal of both males and females was limited to 0.15 km during 45 days after adult emergence. Adults of invasive *Aedes* species are considered weak flyers, with a capacity of dispersal of hundreds of metres based on mark recapture studies (Vavassori et al., 2019). For example, it is known that *Ae. j. japonicus* was unable to expand beyond one tyre recycling centre in Belgium (Damiens et al., 2014). For some vector species (*Anopheles* spp.) related to other diseases such as Malaria, active seasonal migration at high altitude (40–290 m) with displacements of up to 300 km aided by prevalent winds has been described in the Sahel area in Africa(Huestis et al., 2019). In this case, it resulted in a massive movement of mosquitoes (80,000 to 44 million) in a combination with active migration facilitated by prevalent winds. Up until now, such migration behaviour has not been described for the RVFV vector species elsewhere.

For this opinion and according to the assessment conducted by the Vectornet Consortium (Van Bortel et al., 2020), the vector shipped by road transport was considered absent or negligible because, based on the available data, the international annual road freight transport was zero for all countries and over all reporting years. In addition, it was assumed that it is very unlikely that mosquitoes are transported alive from African RVFV at-risk countries to EU MS through wind since because of the long distance (e.g. more than 1000 km from the border of Sudan to Crete).

3.2.1.4. Humans

The great majority of cases of infection with RVFV in humans is asymptomatic. For the small proportion with clinical signs, the majority present with a self-resolving influenza-like syndrome. In some cases, however, RVFV epidemics can involve hundreds of individuals. The manifestation of severe RVF disease cases may include a wide range of clinical signs including hepatitis, retinitis, delayed-onset encephalitis and, in the most severe cases, haemorrhagic disease (Pepin et al., 2010).

Although sick people can develop significant levels of viraemia for a few days (EFSA Panel on Animal Health and Welfare, 2005; Maurice et al., 2018), humans are considered dead-end hosts in the epidemiological cycle of RVF and human–human transmission of the virus has never been described (WHO[18]). Nosocomial transmissions were never reported in Saudi Arabia (Al-Hamdan et al., 2015) or in Egypt during the outbreaks there. However, because nosocomial transmission is theoretically possible, the WHO recommends Standard Precautions in all cases and extra infection control measures to prevent contact with the patient's blood and body fluids and contaminated surfaces or materials such as clothing and bedding, especially in patients affected by haemorrhagic syndromes (WHO).

3.2.2. Selection of relevant pathways

Considering the information presented in Section 3.2.1, the pathways of introduction to be further considered are:

- the movement of infected (pre-viraemic and viraemic) animals (traded or uncontrolled movements) and

[18] https://www.who.int/emergencies/diseases/rift-valley-fever/rvf-presentation.pdf?ua=

- movement of infected vectors by passive movements when shipped by flight, containers or road transport.

These two pathways are considered in the MINTRISK model.

3.2.3. Estimation of parameters to run MINTRISK model

For the estimation of risk of introduction, MINTRISK requires answers to four groups of questions related to RVF: worldwide occurrence, rate of entry, level of transmission and probability of establishment. For each question, an answer provided in a semi-quantitative scale and a related level of uncertainty (low/moderate/high/unknown) should be given. The questions, the values used to answer each of them, and the reasoning is provided in Section 2.2.2.2.

3.2.4. Results of risk of introduction of RVF by MINTRISK model

3.2.4.1. Risk of introduction of RVF into each MS

The MINTRISK model has been used to calculate the scores for the worldwide occurrence, rate of entry, level of transmission and probability of establishment for each MS for both animal and vector pathways (median, lower and upper confidence interval). The score estimates of worldwide occurrence are the same for all MS, given that the same input was used for the area of origin of RVF. It is low for the animal pathway (median 0.3; CI 0.16–0.45) and high for the vector pathway (median 0.7; CI 0.43–0.97).[19]

The rate of entry for the animal pathway in all MS is close to zero, because the number of imported animals is also close to zero. For the vector pathway, the results combined for both air and maritime transport are shown in Figure 10. The entry score (sc) translates into rate of entry (number of entries/year) using the following formula Rate of entry = 10^[5 * (sc-1)] as indicated in (EFSA Panel on Animal Health and Welfare, 2017).

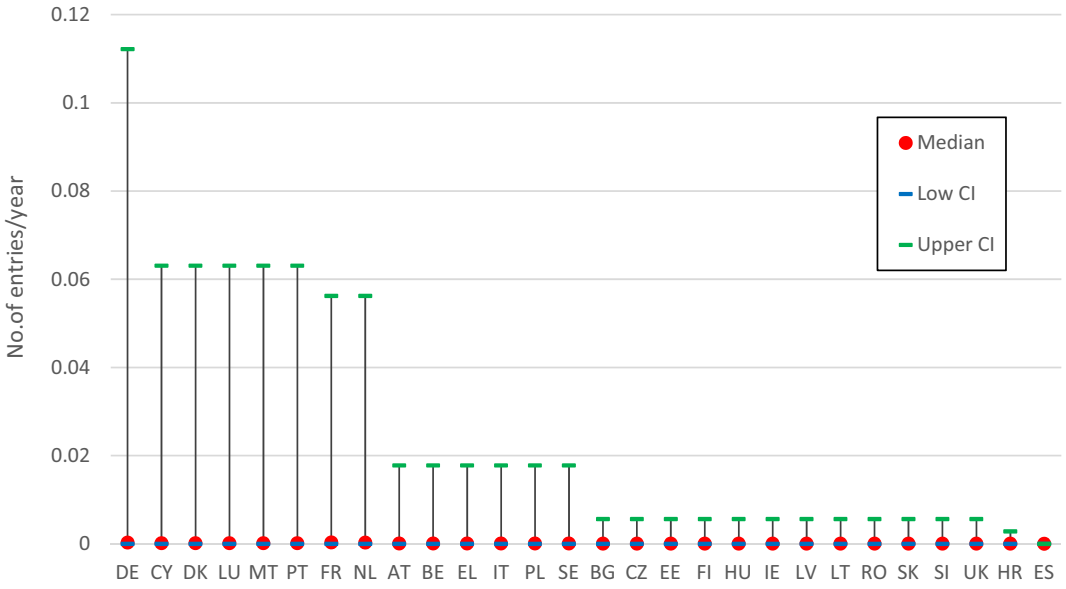

Figure 10: Rate of entry of RVF for the vector pathway (for country codes see Glossary)

Figure 10 shows the median values and the confidence intervals. The median values are close to zero (see Annex A.5 for exact values). The highest values of the rate of entry have been assessed for France (median: 0.000282 introductions/year, CI: $8.9*10^{-7}$; 0.056), Germany (median: 0.000251 introductions/year; CI: $3.9*10^{-7}$; 0.11) and the Netherlands (median: 0.000251 introductions/year; CI: 10^{-6}; 0.056), with Germany having the highest upper confidence interval (0.11 entries/year). Tit should be noted that 0.05 entries/year would correspond to one entry every 20 years (reciprocal number). The higher values for entry are due to the greater number of connections by air and sea

[19] See Annex 10.4 for categorisation of scores in MINTRISK.

transports with African RVF-infected countries. Considering the upper confidence interval (linked to uncertainty), other countries like Cyprus, Denmark, Luxembourg, Malta, Portugal showed greater rates of entry of vectors up to 0.06 entries/year (see Annex A.1 for details on calculation of number of imported vectors). It should also be noted that these uncertainty levels are derived from a series of components linked to the air and sea connection between an affected country and MSs and they are not related to the situation for mosquito survival or abundance within the country (e.g. Denmark or Luxemburg). The major components that influence the levels of uncertainty in the estimation of rate of entry among the countries are the maritime connections (not only air connection) that have a higher uncertainty due to the major uncertainty for this pathway for survival of mosquitoes at destination. Further details are provided in the report by Vectornet (ref to be added).

The qualitative score of the entry of vectors (estimated based on median values, for the assignment of qualitative categories see Annex A.4) is considered 'very low' or 'low' in all MSs (Table 10).

The level of transmission linked to the presence of vectors in MS, R0 and proportion of susceptible animals is estimated as 'moderate' in all MSs (the transmission score translated into reproduction ratio (R0) would give a median value of 1.77 (0.47–6.68) for both animal and vector pathways).

The results of the probability of establishment for the animal and vector pathways are shown in Figure 11. The establishment score presented in Annex A.5 translates into establishment probability using the following formula: Establishment_Probability = 10^[5 x (score-1)] as indicated in (EFSA Panel on Animal Health and Welfare, 2017).

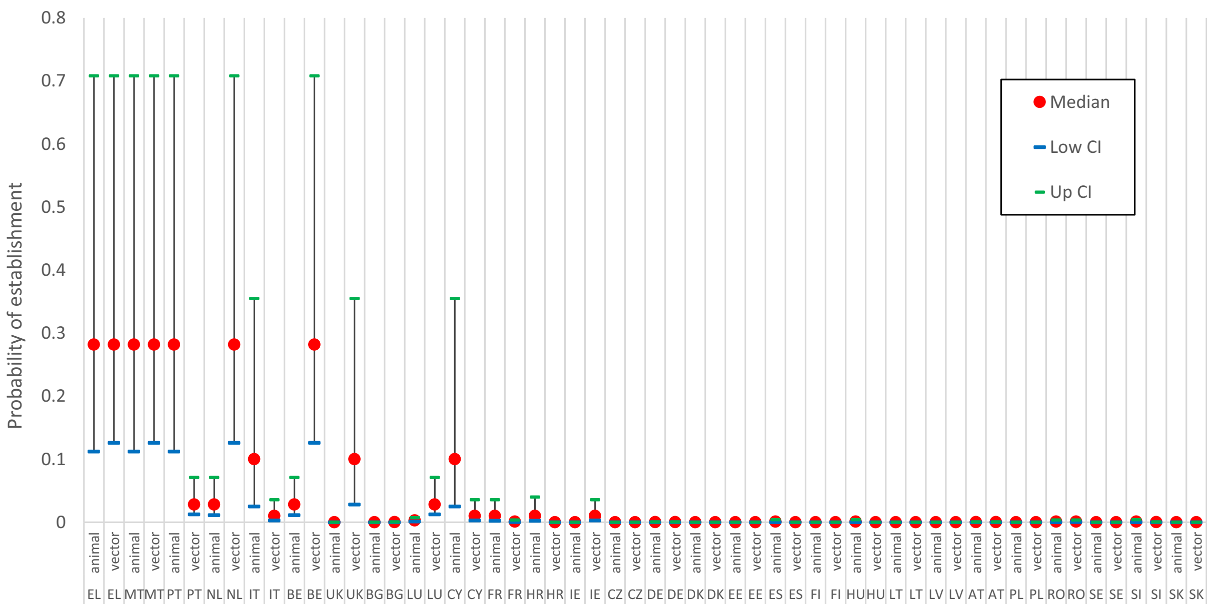

Figure 11: Probability of establishment of RVF in each MS for animal and vector pathway

The probability of the establishment of RVFV transmission, once introduced, varies among the EU MS according to the introduction pathway considered. The scores in Figure 11 are influenced by the host density, the presence of the vectors and in particular by the temperatures that allow vector activity (see Section 2.2.2.2), leading to higher scores in the southern MS compared with northern EU.

Considering the qualitative assessment of the probability of the establishment as in Table 10, for the introduction through infected animals, the highest probability of RVFV establishment ('very high', median: 0.28, CI:0.11–0.71), has been assessed for Greece, Malta and Portugal, followed by 'high to very high' for Cyprus (median: 0.1, CI:0.02–0.35) and Italy (median: 0.1, CI:0.02–0.35), 'high' for Belgium (median: 0.028, CI:0.01–0.071) and the Netherlands (median: 0.028, CI:0.011–0.071), moderate to high for Croatia (median: 0.01, CI:0.002–0.039) and France (median: 0.01, CI:0.002–0.035). For the introduction through infected vectors, 'very high' probability of RVFV transmission establishment is assessed for Belgium (median: 0.28, CI:0.12–0.70), Greece (median: 0.28, CI:0.12–0.70), Malta (median: 0.28, CI:0.12–0.70) and the Netherlands (median: 0.28, CI:0.12–0.70), 'high to very high' for United Kingdom (median: 0.1; CI 0.028–0.35), 'high' probability is reported for Luxembourg, Portugal (median: 0.028; CI: 0.012; 0.07); 'moderate to high' for Cyprus, Ireland, Italy (median: 0.01; CI: 0.0028; 0.035). The

uncertainty on the true values of the parameters used for establishing the probability of establishment was set as low in all MS. However, the range included in the confidence intervals around the estimates, derived from the stochastic calculation done by MINTRISK, was wide enough to contain in certain cases more than one qualitative category (see Annex A.5).

The qualitative results of the assessment of the probability of establishment are shown in Table 10.

The score of the overall risk of introduction has been calculated through the MINTRISK model by combining the rate of entry, level of transmission and probability of establishment. For clarity, it can be expressed as the number of expected RVF epidemics/year by the following formula (EFSA Panel on Animal Health and Welfare, 2017)):

$$\text{No. epidemics/year} = 10\text{^}[5 \times (\text{MINTRISK score} - 0.8)]$$

The results of this are shown in the graph in Figure 12.

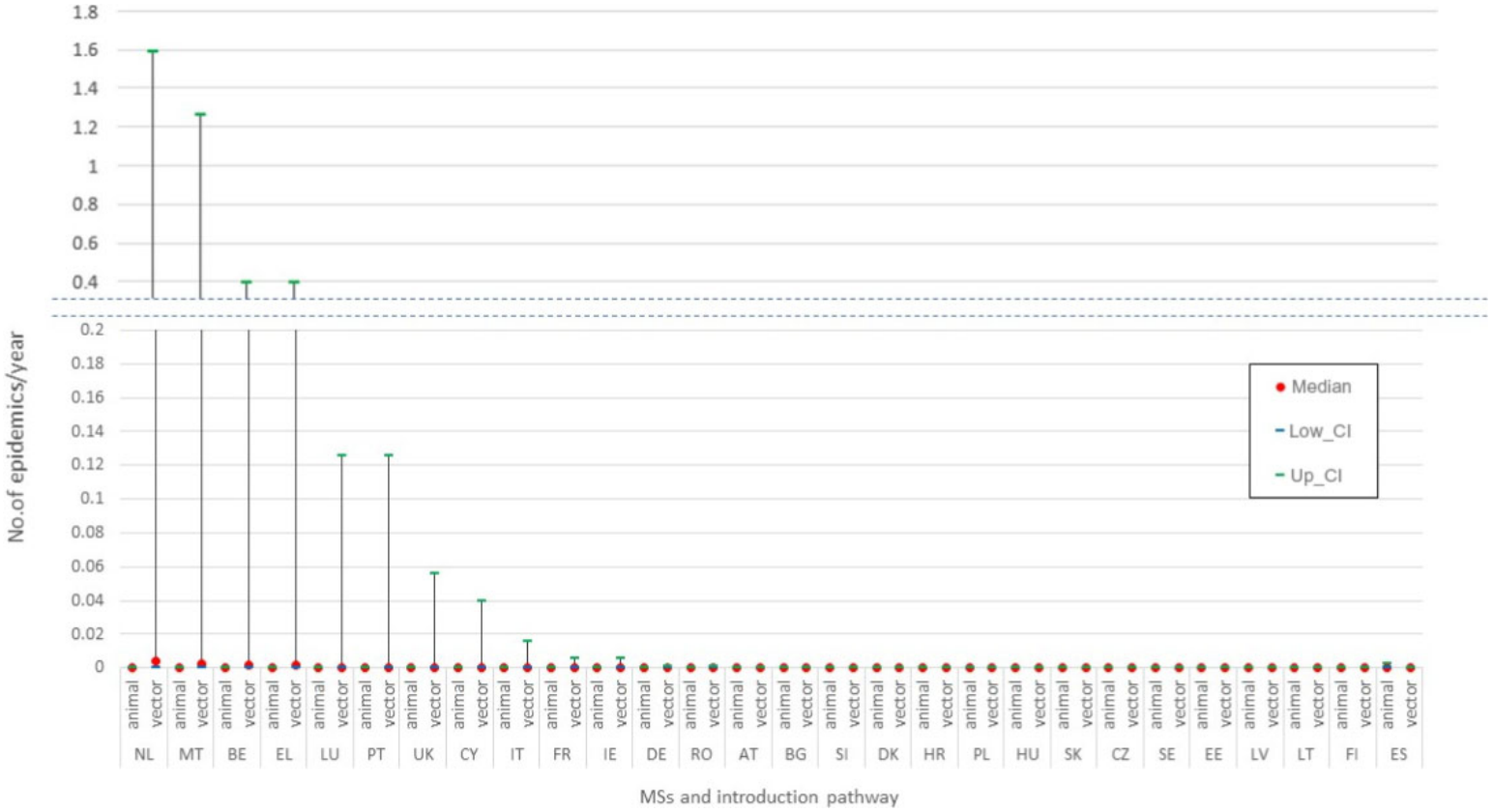

Figure 12: Overall risk of introduction: estimated number of no. epidemics/year of RVF in the MSs by MINTRISK

From the graph in Figure 10, it can be observed that for the animal pathway the risk of introducing RVF is very low (not zero because of the uncertainty in the stochastic calculation), with a highest median value of epidemics/year of $7*10^{-6}$ for Spain and still 0.002 epidemics/year considering the upper confidence interval. This may be due to the strict EU policy on animal import from extra-EU territories and border checks.

On the other hand, for the vector pathway, due to the number of air and sea connections with RVF affected countries, when considering the median values, the highest value is registered for the Netherlands with 0.0044 epidemics/year, meaning one epidemic every 227 years, followed by Malta with 0.0025 epidemics/year (one epidemics every 400 years), Belgium and Greece (0.0014 epidemics/year, one epidemic every 700 years). In the worst-case scenario and considering the uncertainty around these values (upper confidence interval), some MS may have higher risk of RVF introduction of one epidemic every 20 years (Belgium, Greece, Luxemburg, Portugal and UK) upper confidence interval 0.04 epidemics/year, Figure 10), and the Netherlands and Malta may have one epidemic per year (upper CI above 1, Figure 10). This may be linked to the number of connections by air and sea transport that may lead to introducing positive RVF vectors from affected areas. According to the median values, MINTRISK elaborates the qualitative scores (see Annex A.4).

Table 10 shows the results of the qualitative categorisation of MINTRISK outputs for the different components of the risk of introduction and the overall score for each MS (For the numeric scores, see Annex A.5)

Table 10: Qualitative model outputs of entry, transmission and overall introduction RVF for each MSs

Country	Entry score		Level of transmission		Establishment		Overall score of introduction	
pathways	animal	vector	animal	vector	animal	vector	animal	vector
AT	very low	very low	moderate	moderate	very low/low	very low/low	very low	very low
BE	very low	very low	moderate	moderate	high	very high	very low	very low/low
BG	very low	very low	moderate	moderate	very low	very low/low	very low	very low
HR	very low	very low	moderate	moderate	moderate/high	very low	very low	very low
CY	very low	very low/low	moderate	moderate	high/very high	moderate/high	very low	very low
CZ	very low	very low	moderate	moderate	very low	very low	very low	very low
DK	very low	very low/low	moderate	moderate	very low	very low	very low	very low
EE	very low	very low	moderate	moderate	very low	very low	very low	very low
FI	very low	very low	moderate	very low	very low	very low	very low	very low
FR	very low	very low/low	moderate	moderate	moderate/high	low/moderate	very low	very low
DE	very low	very low/low	moderate	moderate	very low/low	very low/low	very low	very low
EL	very low	very low	moderate	moderate	very high	very high	very low	very low/low
HU	very low	very low	moderate	moderate	low/moderate	very low	very low	very low
IE	very low	very low	moderate	moderate	very low	moderate/high	very low	very low
IT	very low	very low	moderate	moderate	high/very high	moderate/high	very low	very low
LV	very low	very low	moderate	moderate	very low	very low	very low	very low
LT	very low	very low	moderate	moderate	very low	very low	very low	very low
LU	very low	very low	moderate	moderate	moderate	high	very low	very low
MT	very low	very low/low	moderate	moderate	very high	very high	very low	very low/low
NL	very low	very low/low	moderate	moderate	high	very high	very low	very low/low
PL	very low	very low	moderate	moderate	very low	very low	very low	very low
PT	very low	very low/low	moderate	moderate	very high	high	very low	very low
RO	very low	very low	moderate	moderate	low/moderate	low/moderate	very low	very low
SK	very low	very low	moderate	moderate	very low	very low	very low	very low
SI	very low	very low	moderate	moderate	low/moderate	very low/low	very low	very low
ES	very low/low	very low	moderate	moderate	low/moderate	very low	very low	very low
SE	very low	very low	moderate	moderate	very low	very low	very low	very low
UK	very low	very low	moderate	moderate	very low	high/very high	very low	very low

3.2.4.2. Risk of introduction of RVF into EU regions

According to the methodology described in Section 2.2.2, the risk of introduction for both vector and animal pathways for the four EU regions considered in the previous EFSA opinion on vector-borne disease (EFSA Panel on Animal Health and Welfare, 2017) results as in Figure 13.

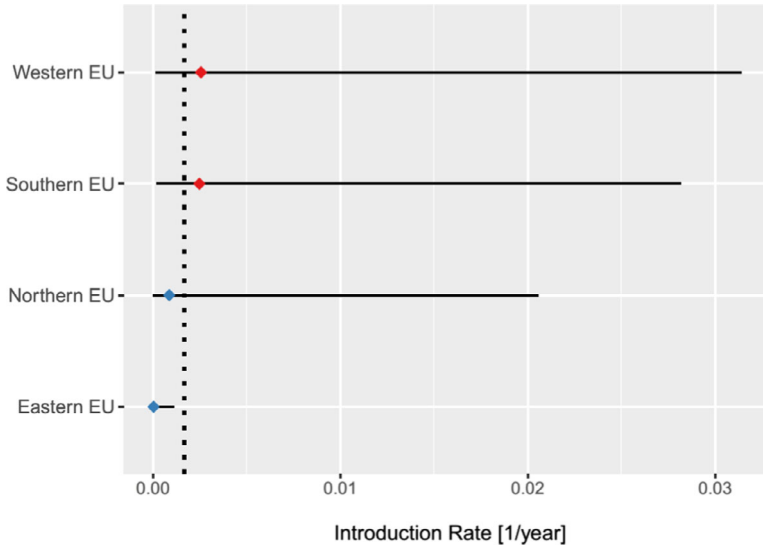

Figure 13: Overall introduction rate for the four EU regions

The values reported in the graph are as below:

- Southern region (Spain, Greece, Malta, Italy, Croatia, Slovenia, Portugal, Cyprus): median: 0.002; CI: $1.84*10^{-4}$-0.028;
- Western region (Belgium, the Netherlands, Luxembourg, France, Germany, Austria): median: 0.002; CI: $1.35*10^{-4}$;0.03;
- Northern region (Lithuania, Denmark, Latvia, Ireland, Finland, Estonia, Sweden, United Kingdom): median: 0.00086; CI: $1.22*10^{-5}$;0.0205;
- Eastern region (Hungary, Poland, Czechia, Bulgaria, Slovakia, Romania): median: $2.8*10^{-5}$; CI: $5.71*10^{-7;}$ 0.0011.

According to the categorisation as form the MINTRISK model (Annex A.4), all the regions would be categorised as having a very low risk of introduction of RVF, even considering the upper bound, that is still below 0.15 (threshold value for 'very low', Annex A.4).

4. Conclusions

ToR 1.1. Global epidemiological situation of RVF

Virus

- RVFV consists of a single serotype of the genus *Phlebovirus* with a limited genomic variability among the circulating strains. The virus is readily inactivated by lipid solvents and acid conditions (pH < 6)

Spatial temporal distribution

- RVF has been historically present in sub-Saharan areas and in specific zones of the Arabian Peninsula, in the border between Saudi Arabia and Yemen.
- In the last two decades, more evidence has been observed on the spread of RVFV into new African areas not regarded as infected before, even in areas considered not optimal for mosquito-borne diseases, like the pre-desertic areas of Sahel.
- Historically major RVF epidemics have been cyclically observed in endemic areas, with long inter-epizootic periods (5–15 years) during which the virus was not detected in animal populations. In the last decade, RVF epidemics have been recorded more frequently and low-level enzootic RVFV circulation in livestock has been demonstrated in various areas.

- There have been recent outbreaks in French overseas departments and seropositive cases detected in Turkey, Tunisia and Libya, what has raised concerns on the potential risk for introduction into neighbouring EU countries.
- Positive serological findings in Algeria, Western Sahara, Tunisia, Libya, Iraq, Iran, Turkey, which are countries considered officially free from RVF, must be carefully interpreted on the bases of the study designs and diagnostic tests used. However, the detection of serological positive individuals (animals or humans) in these countries must be seen as a signal of a potential risk of RVF spread out of its endemic geographical area.

Transmission

- RVFV transmission is driven by several species of mosquitoes. Species belonging to *Aedes* and *Culex* genus are the most relevant for enzootic and epizootic cycles, respectively.
- Epizootic transmission is favoured by particular climatic conditions, such as heavy rains.
- Vertical transmission of the virus has been described in one species of vectors; however, its role on the survival of the virus during inter-epizootic periods remains unclear.

Possible expansion of RVF

- The movement of live animals is the main risk factor for RVF spread from the African endemic areas.
- Several pathways of livestock movements between sub-Saharan and North African countries can be identified. It is reasonable to assume that a large part of these cross-borders movements is currently not subjected to veterinary checks.
- The trade from the Horn of Africa towards the Arabian Peninsula and Middle East involves several million live animals each year, thus representing a constant risk of RVF introduction into the Middle East.

Diagnosis

- Molecular assays are available to detect RVFV, including DIVA test (gel-based and RT PCR).
- Serological tests are available to detect RVF antibodies and to distinguish early from past infection of RVF in domestic ruminants.
- In the EU, the diagnostic capacity of the laboratories has been assessed and the level of performance considered adequate, as well as in National Laboratories from Algeria, Mauritania, Morocco, Tunisia, Mali and Senegal.
- RVF diagnostic tests are in place in most of the other Mediterranean countries; nevertheless, an evaluation of their performances should be encouraged through inter laboratory trials.

Vaccines

- No vaccines have been authorised for use in the EU. Their use for emergency vaccination should be on an ad hoc basis and authorised following the proper EU procedure.
- Both live-attenuated and inactivated vaccines are commercially available for RVF and have contributed significantly to the control of RVF in endemic countries. However, they require repeated vaccinations (inactivated vaccines) and retain the risk for teratogenic effects, abortion and potential reassortment/reversion to virulence (live attenuated).
- Several novel candidate vaccines are in the final stages of validation and, among them, most allow the discrimination of naturally infected from vaccinated animals (DIVA).
- Preventive mass vaccination is the most effective means to control RVF circulation when climatic, environmental and epidemiological evaluations suggest a high probability of RVF outbreaks. However, the use of vaccines should be carefully evaluated once the virus transmission has already been detected in the area since it may intensify transmission among herds through needle propagation of the virus.

TOR 1.2 and 1.3 Risk of introduction into EU

Pathways of possible introduction of RVF into EU

- Among the possible pathways for RVF introduction into the EU, the movements of infected animals (traded or uncontrolled movements) and movements of infected vectors by active flight or their passive movements when shipped by flight, containers or road transport are considered as plausible pathways of introduction and were further considered in the assessment.

Rate of entry

- The rate of RVFV entry into the EU MS through the entry of infected animals was assessed by MINTRISK scale as 'very low', whereas the entry of infected vectors was considered 'very low' or 'low'. In particular, the highest values of the rate of entry have been assessed for France (median: 0.000282 entries/year; CI: $8.9*10^{-7}$; 0.056), Germany (median: 0.000251 entries/year; CI: $3.9*10^{-7}$; 0.11) and the Netherlands (median: 0.000251 entries/year; CI: 10^{-6}; 0.056), due to the greater number of connections by air and sea transport with African RVF-infected countries.
- Due to the level of uncertainty, further countries (Cyprus, Denmark, Luxembourg, Malta, Portugal) showed greater rates of entry of vectors (up to 0.06 entries per year) when the upper 95% confidence values are considered. This level of uncertainty is linked to the number of air and sea connections between affected country and MSs, especially the maritime connections generate higher uncertainty for the survival of mosquitoes at destination.

Level of transmission

- For all MS, a 'moderate' level of transmission (R0) has been assessed (median value 1.77; CI: 0.47–6.68). In fact, the input variables for the estimation of this parameter (distribution of vectors in the countries, estimated value of the basic reproduction ratio**,** fraction of the host population being susceptible) are the same for all MSs.

Probability of establishment

- The probability of the establishment of RVFV transmission, once introduced, varies among the EU MS according to the introduction pathway considered:
    - For the introduction through infected animals, a 'very high' probability (median: 0.28, CI: 0.11–0.71) of RVFV transmission establishment has been assessed for Greece, Malta and Portugal, 'high to very high' for Cyprus (median: 0.1, CI: 0.02–0.35) and Italy (median: 0.1, CI: 0.02–0.35); 'high' probability is considered for Belgium (median: 0.028, CI: 0.01–0.071) and the Netherlands (median: 0.028, CI: 0.011–0.071); 'moderate to high' for Croatia (median: 0.01, CI: 0.002–0.039) and France (median: 0.01, CI: 0.002–0.035).
    - For the introduction through infected vectors, 'very high' probability of RVFV transmission establishment is assessed for Belgium (median: 0.28, CI: 0.12–0.70), Greece (median: 0.28, CI: 0.12–0.70), Malta (median: 0.28, CI: 0.12–0.70) and the Netherlands (median: 0.28, CI: 0.12–0.70), 'high to very high' for United Kingdom (median: 0.1; CI: 0.028–0.35), 'high' probability is reported for Luxembourg, Portugal(median: 0.028; CI: 0.012; 0.07); 'moderate to high' for Cyprus, Ireland, Italy (median: 0.01; CI: 0.0028; 0.035). The uncertainty around those values comprised in certain cases more than one qualitative category.
- The differences observed between the probability estimates of the two introduction pathways (animal or vector) are mainly due to differences in host density between the countries, and the climatic conditions, which are inputs for the estimation of probability of the first transmission step following the introduction of infected vectors.

Overall rate of introduction

- Although the results of the assessment indicate that the risk of RVFV introduction into the EU is currently very low, higher risk values have been estimated following the introduction of infected vectors.
- For the animal pathway, the risk of RVF introduction into the EU is very low for all the EU MSs (less than 0.002 epidemics/year, i.e. one epidemic every 500 years, as the worst-case scenario, the highest upper confidence level estimated), given the strict health policy in place in the EU on the import of live animals from RVF infected Third Countries and due the long distance between the countries actually infected by RVF and the EU borders.
- For the vector pathway, the risk is very low for the great majority of MSs, but it is very low to low, when considering the median values, for Netherlands with 0.0044 epidemics/year (CI: $2.51*10^{-5}$; 1.58), meaning one epidemic every 227 years, followed by Malta with 0.0025 epidemics/year (CI: $5.62*10^{-6}$; 0.1.25), Belgium and Greece (0.0014 epidemics/year, CI: $4.47*10^{-6}$; 0.39, one epidemic every 700 years). In the worst-case scenario and considering the uncertainty around these values (upper confidence intervals), some MS may have a higher risk of RVF introduction (0.04 epidemics/year for Belgium, Greece, Luxemburg, Portugal and

UK), and the Netherlands and Malta may have one epidemic per year. This is mainly linked to the number of connections by air and sea transport with African RVF-infected countries.
- Considering the four EU regions, all of them are categorised as at very low risk of introduction of RVF, Southern region (median: 0.002; CI: $1.84*10^{-4}$–0.028), Western (median: 0.002; CI: $1.35*10^{-4}$–0.03); Northern (median: 0.00086; CI: $1.22*10^{-5}$–0.0205); Eastern region (median: $2.8*10^{-5}$; CI: $5.71*10^{-7}$ – 0.0011).

5. Recommendations

- Considering the possible future source of risk represented by the spread of infection into new areas closer to the EU borders, it is of paramount importance for the EU to establish and maintain a close collaboration with North African and Middle Eastern countries in the surveillance of possible introduction of RVF from currently infected areas, as well as to carefully monitor the evolution of the epidemics in African countries.
- Although the EU territory does not seem to be directly exposed to an immediate risk of RVFV introduction, the evolution in the global situation of RVF occurrence, the risk of further spreading of infection into countries closer to the EU borders and the risks linked to the possible introduction of infected vectors, suggest EU authorities to strengthen, improve and harmonise their surveillance and response capacities as well as their scientific and technical expertise to be better prepared in case of RVFV introduction.
- Considering that higher risk values were estimated for the introduction of infected vectors, it is recommended to integrate the surveillance systems already in place in the EU for invasive mosquitoes, taking into account the main possible points of entry of RVFV-infected vectors. Particular attention should be given to those countries receiving major air and sea traffic from RVF-affected countries.
- Despite disinsection procedures being compulsory in some cases and widely recommended by WHO and IATA, it is still important to have additional data about the efficacy of the treatments conducted in airplanes and ships in order to avoid the entry of vectors arriving from RVF-affected countries.
- Considering a possible introduction of RVFV in the EU, information about the potential mosquito vector species associated to livestock premises and the surrounded environment will be essential to develop adequate protocols for vector control.

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Abbreviations

ADNS	Animal Disease Notification System
AGID	agar gel immunodiffusion
CVOs	Chief Veterinary Officers
ELISA	enzyme-linked immunosorbent assay
FMD	foot and mouth disease
LFT	lateral flow test
OIE	World Organisation for Animal Health
PCR	polymerase chain reaction
RPA	recombinase polymerase amplification
RT	reverse transcriptase
RT-LAMP	RT Loop-mediated isothermal amplification
RVF	Rift Valley fever
SIT	Sterile Insect Technique
ToRs	Terms of reference
VNT	Viral neutralisation tests
VT	Vertical transmission
WHO	World Health Organization

EU country codes

Belgium	BE	Greece	EL	Lithuania	LT	Portugal	PT
Bulgaria	BG	Spain	ES	Luxembourg	LU	Romania	RO
Czechia	CZ	France	FR	Hungary	HU	Slovenia	SI
Denmark	DK	Croatia	HR	Malta	MT	Slovakia	SK
Germany	DE	Italy	IT	Netherlands	NL	Finland	FI
Estonia	EE	Cyprus	CY	Austria	AT	Sweden	SE
Ireland	IE	Latvia	LV	Poland	PL	United Kingdom	UK

Annex A

A.1. Estimated number of imported vectors

For combining the values of vectors moved along the two pathways into one, the following is used:

$$(\text{vectors moved by air} * P2_{air}) + (\text{vectors moved by sea} * P2_{sea})^{20}$$

For calculating the uncertainty level for the combined values of vectors moved along both pathways:

$$\text{Let}: UN = upCI, LN = lowCI, UP2 = 97.5\%\ P2 \text{ and } LP2 = 2.5\%\ P2$$

$$\text{Uncertainty} = [(UN_{sea} \times UP2_{sea} + UN_{air} \times UP2_{air}) - (LN_{sea} \times LP2_{sea} + LN_{air} \times LP2_{air})]/2[(N_{sea} \times P2_{sea} + N_{air} \times P2_{air})]$$

Then, the results of uncertainty X are classified as :

$$X <= 0.1 \rightarrow \text{Low}; 0.1 < X <= 0.3 \rightarrow \text{Moderate}; 0.3 < X \rightarrow \text{High}$$

See Table A.1 below for all values (Van Bortel et al., 2020).

Table A.1: Estimated number of imported vectors per type of transport

Country	Transport	No. vector moved/year	Lower CI	Upper CI	Uncertainty	Transport	No. vector moved/ year	Lower CI	Upper CI	Uncertainty	Combined air + sea	Uncertainty category
Austria	sea	0	0	0	0	air	7.619	6.814	8.411	0.1048038	7.344716	moderate
Belgium	sea	4.434	3.934	4.945	0.11400541	air	12.479	10.982	14.037	0.1224056	13.812224	moderate
Bulgaria	sea	0	0	0	0	air	0	0	0	0	0	low
Croatia	sea	0	0	0	0	air	0	0	0	0	0	low
Cyprus	sea	0.017	0.01	0.026	0.47058824	air	0.012	0.006	0.02	0.5833333	0.020459	high
Czechia	sea	0	0	0	0	air	0	0	0	0	0	low
Denmark	sea	0.002	0	0.005	1.25	air	0.012	0.006	0.02	0.5833333	0.01247	high
Estonia	sea	0	0	0	0	air	0	0	0	0	0	low
Finland	sea	0	0	0	0		0	0	0	0	0	low
France	sea	0.885	0.783	0.993	0.11864407	air	601.379	555.043	647.849	0.077161	580.238231	low

[20] See Annex A.2.

Country	Transport	No. vector moved/year	Lower CI	Upper CI	Uncertainty	Transport	No. vector moved/ year	Lower CI	Upper CI	Uncertainty	Combined air + sea	Uncertainty category
Germany	sea	5.327	4.727	5.965	0.11620049	air	858.709	782.014	938.435	0.0910792	829.835717	moderate
Greece	sea	0.052	0.038	0.067	0.27884615	air	0.171	0.141	0.204	0.1842105	0.191364	moderate
Hungary	sea	0	0	0	0	air	0	0	0	0	0	low
Ireland	sea	0	0	0	0	air	0	0	0	0	0	low
Italy	sea	1.115	0.973	1.262	0.12959641	air	98.736	90.738	106.836	0.0815204	95.627504	moderate
Latvia	sea	0	0	0	0	air	0	0	0	0	0	low
Lithuania	sea	0	0	0	0	air	0	0	0	0	0	low
Luxembourg	sea	0	0	0	0	air	0.028	0.018	0.04	0.3928571	0.026992	high
Malta	sea	0.017	0.01	0.026	0.47058824	air	0	0	0	0	0.0068	high
Netherlands	sea	15.504	13.791	17.281	0.1125516	air	770.358	711.589	831.024	0.0775192	748.749192	moderate
Poland	sea	0	0	0	0	air	18.446	16.233	20.773	0.1230619	17.781944	moderate
Portugal	sea	0.17	0.141	0.202	0.17941176	air	0.028	0.018	0.039	0.375	0.112502	high
Romania	sea	0	0	0	0	air	0	0	0.001	0	0	low
Slovakia	sea	0	0	0	0	air	0	0	0.002	0	0	low
Slovenia	sea	0	0	0	0	air	0	0	0	0	0	low
Spain	sea	6.954	6.18	7.761	0.11367558	air	65.534	58.665	72.516	0.105678	67.152464	moderate
Sweden	sea	0	0	0	0	air	0.272	0.21	0.341	0.2408088	0.262208	moderate
UK	sea	0	0	0	0	air	0	0	0	0	0	moderate

A.2. Estimation of mosquito survival in sea and air transport

In Table A.2, the survival of vectors during transport by flight or by sea transport is indicated.

Table A.2: Estimation of mosquito survival in sea and air transport

Country	P2 – probability of survival							
	Air				Maritime			
	mean	2.50%	97.50%	uncertainty level	mean	2.50%	97.50%	uncertainty level
Austria	0.964	0.921	0.983	low				
Belgium	0.964	0.921	0.983	low	0.402	0.128	0.656	high
Bulgaria	0.964	0.921	0.983	low				
Croatia	0.964	0.921	0.983	low	0.794	0.629	0.883	moderate
Cyprus	0.964	0.921	0.983	low	0.523	0.194	0.814	high
Czechia	0.964	0.921	0.983	low				
Denmark	0.964	0.921	0.983	low	0.451	0.196	0.647	high
Estonia	0.964	0.921	0.983	low				
Finland	0.964	0.921	0.983	low				
France	0.964	0.921	0.983	low	0.575	0.258	0.775	high
Germany	0.964	0.921	0.983	low	0.383	0.117	0.632	high
Greece	0.964	0.921	0.983	low	0.51	0.189	0.795	high
Hungary	0.964	0.921	0.983	low				
Ireland	0.964	0.921	0.983	low	0.506	0.247	0.689	high
Italy	0.964	0.921	0.983	low	0.4	0.141	0.646	high
Latvia	0.964	0.921	0.983	low				
Lithuania	0.964	0.921	0.983	low				
Luxembourg	0.964	0.921	0.983	low				
Malta	0.964	0.921	0.983	low	0.4	0.141	0.646	high
Netherlands	0.964	0.921	0.983	low	0.395	0.127	0.633	high
Poland	0.964	0.921	0.983	low				
Portugal	0.964	0.921	0.983	low	0.503	0.194	0.759	high
Romania	0.964	0.921	0.983	low	0.794	0.629	0.883	moderate
Slovakia	0.964	0.921	0.983	low				
Slovenia	0.964	0.921	0.983	low	0.794	0.629	0.883	moderate
Spain	0.964	0.921	0.983	low	0.572	0.263	0.779	high
Sweden	0.964	0.921	0.983	low	0.399	0.154	0.607	high
United Kingdom	0.964	0.921	0.983	low	0.425	0.146	0.661	high

A.3. Host density, vector presence and proportion of days above temperature threshold of 9.6°C

The three components are estimated as below:

- **Vector:** proportion of the country with any predicted RVF vector presence (Wint et al., 2020).
- **Host:** proportion of the country where the sum of density for sheep + goats + cattle > 50 animals/sqKM, or any of three deer species > 90% of probability of presence.
- **Temperature:** mean daily temperature averaged of 2013–2018 per each MS capital city, calculate the proportion of days above 9.6°C per each MS out of the total number of days in 5 years.

In Table A.3, the estimated parameters are presented.

Table A.3: Host density category, vector presence and temperature classes in all MS, and probability of first and second transmission step of RVF

Country	Ruminants	Area	Density	Density_ category	proportion country with vector presence	% days above 9.6°C	Probability first transmission step vectors	Probability first transmission step cat vect	Probability first transmission step animals	Probability first transmission step cat animals	Probability second transmission step - combined T°C, vector and host	Probability second transmission step category
Austria	2,422,310	83738.8450	28.9269574	0.019622181	0.804780876	0.626	0.110830886	moderate	0.709783649	moderate	0.214618137	Moderate
Belgium	2,640,170	30479.6110	86.6208562	0.058757999	0.998078155	0.606	0.188699092	very high	0.777711619	high	0.328776971	Very High
Bulgaria	2,209,260	110801.4860	19.9389023	0.013525265	0.905093066	0.6	0.090084176	low	0.736923225	moderate	0.1943853	Low
Croatia	1,296,270	56287.7890	23.0293288	0.01562161	0.988340459	0.619	0.098335024	low	0.78216542	very high	0.212214152	Moderate
Cyprus	488,490	9251.0000	52.8040212	0.03581884	0.741144414	0.888	0.178345536	high	0.811255964	very high	0.286731743	High
Czechia	1,662,640	78495.1740	21.1814296	0.014368115	0.412844037	0.537	0.08783893	low	0.470847372	very low	0.147136368	Very Low
Denmark	1,728,520	42670.7140	40.5083449	0.027478247	0.47323601	0.505	0.117798619	moderate	0.488860087	low	0.187263324	Low
Estonia	353,410	45544.5590	7.75965357	0.005263648	0.471465871	0.399	0.045827891	very low	0.433722126	very low	0.099671273	Very Low
Finland	1,070,320	333796.9510	3.20650023	0.002175083	0.050325707	0.4	0.029496324	very low	0.141881228	very low	0.035245896	Very Low
France	26,782,730	546728.9350	48.9872189	0.033229768	0.84562534	0.667	0.148876644	moderate	0.751020707	high	0.265629952	High
Germany	14,348,990	356108.7820	40.2938392	0.02733274	0.887859129	0.532	0.120586142	moderate	0.68727073	moderate	0.23459187	Moderate
Greece	12,389,010	131851.8520	93.9615926	0.063737481	0.899341142	0.873	0.235887305	very high	0.886072693	very high	0.368505974	Very High
Hungary	2,161,250	92782.1970	23.2938006	0.015801011	0.997734481	0.592	0.096717106	low	0.768543306	high	0.210542862	Low
Ireland	12,371,770	69384.1640	178.308266	0.120952821	0.155685441	0.545	0.256747517	very high	0.291287771	very low	0.217313564	Moderate
Italy	14,123,050	300979.4500	46.9236355	0.031829966	0.861845085	0.855	0.164968546	high	0.85841572	very high	0.286248905	High
Latvia	578,800	64298.8910	9.00171046	0.006106179	0.662634762	0.45	0.052419278	very low	0.546063772	low	0.122110244	Very Low
Lithuania	941,180	64849.1990	14.5133635	0.009844929	0.9626703	0.454	0.066855051	very low	0.661099324	moderate	0.16264798	Very Low
Luxembourg	215,500	2594.1160	83.0726151	0.056351101	1	0.546	0.175407244	high	0.738918128	moderate	0.313351431	Very High

Country	Ruminants	Area	Density	Density_ category	proportion country with vector presence	% days above 9.6°C	Probability first transmission step vectors	Probability first transmission step cat vect	Probability first transmission step animals	Probability first transmission step cat animals	Probability second transmission step - combined T°C, vector and host	Probability second transmission step category
Malta	32,400	332.3660	97.4828954	0.066126105	1	0.996	0.256635151	very high	0.997997996	very high	0.403841327	Very High
Netherlands	5,534,930	35492.6890	155.945637	0.105783456	0.983723296	0.582	0.248124911	very high	0.756655112	high	0.392709341	Very High
Poland	6,248,900	310715.0620	20.1113521	0.013642243	0.798083964	0.514	0.083738361	low	0.640480411	low	0.177541206	Low
Portugal	4,156,760	91280.7050	45.538211	0.030890183	0.917357513	0.972	0.17327798	high	0.944283592	very high	0.302001054	Very High
Romania	12,328,610	236654.0270	52.0955006	0.035338226	0.86885691	0.63	0.149208184	moderate	0.739851237	moderate	0.268438322	High
Slovakia	842,930	48648.3070	17.3270161	0.01175353	0.713330547	0.576	0.08228021	low	0.640997968	low	0.169028733	Low
Slovenia	659,500	20245.6890	32.5748361	0.022096667	0.988247863	0.613	0.116384091	moderate	0.778328941	high	0.237438445	Moderate
Spain	24,443,430	498117.6110	49.0716037	0.033287009	0.473981425	0.715	0.154273172	high	0.582148365	low	0.224274921	Moderate
Sweden	2,067,070	443799.6830	4.65766444	0.003159459	0.121711358	0.432	0.036944367	very low	0.229301781	very low	0.054972125	Very Low
United Kingdom	43,049,890	243137.1760	177.060089	0.120106138	0.289522399	0.646	0.27854724	very high	0.432471351	very low	0.282158603	High

A.4. Assignment of qualitative categories by MINTRISK

The assignment of qualitative categories to the computed scores by MINTRISK and when transformed into rate of entry, probability of establishment and overall risk of introduction is in Table A.4.

Table A.4: Assignment of qualitative categories to the computed scores by MINTRISK

Risk level	scores as computed by MINTRISK		Rate of entry and probability of establishment		overall risk of introduction	
	Lower boundary	Upper boundary	Lower boundary	Upper boundary	Lower boundary	Upper boundary
Very low	<	0.15	<	5.62E-05	<	0.000562
Very low/low	0.15	0.25	5.62E-05	0.000178	0.000562	0.001778
Low	0.25	0.35	0.000178	0.000562	0.001778	0.005623
Low/moderate	0.35	0.45	0.000562	0.001778	0.005623	0.017783
Moderate	0.45	0.55	0.001778	0.005623	0.017783	0.056234
Moderate/high	0.55	0.65	0.005623	0.017783	0.056234	0.177828
High	0.65	0.75	0.017783	0.056234	0.177828	0.562341
High/very high	0.75	0.85	0.056234	0.177828	0.562341	1.778279
Very high	>	0.85	>	0.177828	>	1.778279

A.5. MINTRISK outputs for the scores of entry, transmission, establishment and overall score of introduction

In Table A.5 below, the MINTRISK scores are reported.

A score of 1 translates to 10 epidemics starting each year, a score of 0.8 translates to one epidemic per year, 0.6 translates to 1 epidemic every 10 years etc. The overall introduction score (sc) translates into the number of new epidemics/year (No. epidemics/year) using the following formula: No. epidemics/year = 10^[5 * (score-0.8)].

Table A.5: MINTRISK scores calculated for RVF introduction into MSs

Country	Entry score		Level of transmission		Establishment		Overall score of introduction	
pathways	animal	vector	animal	vector	animal	vector	animal	vector
AT	−0.8 (−0.99; −0.59)	0.14 (−0.37; 0.65)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.2 (0.08; 0.32)	0.2 (0.09; 0.31)	−1.39 (−1.62; −1.16)	−0.46 (−0.97; 0.05)
BE	−0.8 (−0.99; −0.59)	0.14 (−0.37; 0.65)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.69 (0.61; 0.77)	0.89 (0.82; 0.97)	−0.91 (−1.12; −0.68)	0.23 (−0.27; 0.72)
BG	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0 (−0.12; 0.12)	0.2 (0.09; 0.31)	−1.59 (−1.82; −1.36)	−0.52 (−1.02; −0.03)
HR	−0.8 (−0.99; −0.59)	0.09 (−0.35; 0.49)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.6 (0.48; 0.72)	0 (−0.11; 0.11)	−0.99 (−1.22; −0.76)	−0.72 (−1.16; −0.3)
CY	−0.8 (−0.99; −0.59)	0.21 (−0.34; 0.76)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.8 (0.68; 0.91)	0.6 (0.49; 0.71)	−0.8 (−1.02; −0.56)	0 (−0.54; 0.52)
CZ	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	−0.6 (−0.72; −0.48)	−0.4 (−0.51; −0.29)	−2.19 (−2.4; −1.96)	−1.12 (−1.62; −0.63)

Country	Entry score		Level of transmission		Establishment		Overall score of introduction	
pathways	animal	vector	animal	vector	animal	vector	animal	vector
DK	−0.8 (−0.99; −0.59)	0.21 (−0.34; 0.76)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	−0.2 (−0.32; −0.08)	0 (−0.11; 0.11)	−1.79 (−2.02; −1.56)	−0.6 (−1.14; −0.04)
EE	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	−0.6 (−0.72; −0.48)	−0.6 (−0.71; −0.49)	−2.19 (−2.4; −1.96)	−1.32 (−1.82; −0.83)
FI	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	−1.33 (−1.89; −0.98)	−0.6 (−0.72; −0.48)	−0.6 (−0.71; −0.49)	−2.19 (−2.4; −1.96)	−1.45 (−1.93; −1.09)
FR	−0.8 (−0.99; −0.59)	0.29 (−0.21; 0.75)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.6 (0.48; 0.71)	0.4 (0.29; 0.51)	−1 (−1.22; −0.76)	−0.12 (−0.62; 0.35)
DE	−0.8 (−0.99; −0.59)	0.28 (−0.28; 0.81)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.2 (0.08; 0.32)	0.2 (0.09; 0.31)	−1.39 (−1.62; −1.16)	−0.33 (−0.86; 0.21)
EL	−0.8 (−0.99; −0.59)	0.14 (−0.37; 0.65)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.89 (0.81; 0.97)	0.89 (0.82; 0.97)	−0.71 (−0.92; −0.48)	0.23 (−0.27; 0.72)
HU	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.4 (0.28; 0.52)	−0.2 (−0.31; −0.09)	−1.19 (−1.42; −0.96)	−0.92 (−1.42; −0.43)
IE	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	−0.2 (−0.32; −0.08)	0.6 (0.49; 0.71)	−1.79 (−2.02; −1.56)	−0.12 (−0.62; 0.35)
IT	−0.8 (−0.99; −0.59)	0.14 (−0.37; 0.65)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.8 (0.68; 0.91)	0.6 (0.49; 0.71)	−0.8 (−1.02; −0.56)	−0.06 (−0.57; 0.44)
LV	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	−0.4 (−0.52; −0.28)	−0.6 (−0.71; −0.49)	−1.99 (−2.22; −1.76)	−1.32 (−1.82; −0.83)
LT	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	−0.2 (−0.32; −0.08)	−0.6 (−0.71; −0.49)	−1.79 (−2.02; −1.56)	−1.32 (−1.82; −0.83)
LU	−0.8 (−0.99; −0.59)	0.21 (−0.34; 0.76)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.49 (0.41; 0.57)	0.69 (0.62; 0.77)	−1.11 (−1.32; −0.88)	0.1 (−0.45; 0.62)
MT	−0.8 (−0.99; −0.59)	0.21 (−0.34; 0.76)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.89 (0.81; 0.97)	0.89 (0.82; 0.97)	−0.71 (−0.92; −0.48)	0.28 (−0.25; 0.82)
NL	−0.8 (−0.99; −0.59)	0.28 (−0.2; 0.75)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.69 (0.61; 0.77)	0.89 (0.82; 0.97)	−0.91 (−1.12; −0.68)	0.33 (−0.12; 0.84)
PL	−0.8 (−0.99; −0.59)	0.14 (−0.37; 0.65)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	−0.2 (−0.32; −0.08)	−0.2 (−0.31; −0.09)	−1.79 (−2.02; −1.56)	−0.86 (−1.37; −0.35)
PT	−0.8 (−0.99; −0.59)	0.21 (−0.34; 0.76)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.89 (0.81; 0.97)	0.69 (0.62; 0.77)	−0.71 (−0.92; −0.48)	0.1 (−0.45; 0.62)
RO	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.4 (0.28; 0.51)	0.4 (0.29; 0.51)	−1.2 (−1.42; −0.96)	−0.32 (−0.82; 0.17)
SK	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	−0.2 (−0.32; −0.08)	−0.2 (−0.31; −0.09)	−1.79 (−2.02; −1.56)	−0.92 (−1.42; −0.43)

Country	Entry score		Level of transmission		Establishment		Overall score of introduction	
pathways	animal	vector	animal	vector	animal	vector	animal	vector
SI	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.4 (0.28; 0.52)	0.2 (0.09; 0.31)	−1.19 (−1.42; −0.96)	−0.52 (−1.02; −0.03)
ES	0.17 (−0.3; 0.66)	−0.8 (−0.99; −0.58)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0.4 (0.28; 0.52)	0 (−0.11; 0.11)	−0.23 (−0.71; 0.28)	−1.6 (−1.82; −1.37)
SE	−0.8 (−0.99; −0.59)	0.14 (−0.37; 0.65)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	−0.6 (−0.72; −0.48)	−0.6 (−0.71; −0.49)	−2.19 (−2.4; −1.96)	−1.26 (−1.77; −0.75)
UK	−0.8 (−0.99; −0.59)	0.09 (−0.41; 0.55)	0.5 (0.27; 0.73)	0.5 (0.27; 0.74)	0 (−0.12; 0.11)	0.8 (0.69; 0.91)	−1.6 (−1.82; −1.36)	0.08 (−0.42; 0.55)