RAPID RISK ASSESSMENT

Clusters of autochthonous chikungunya cases in Italy

First update

9 October 2017

Conclusions and options for response

Italy is currently experiencing four clusters of autochthonous chikungunya cases in the cities of Anzio, Latina and Rome in the Lazio region, and the city of Guardavalle Marina in the Calabria region. Autochthonous transmission of mosquito-borne infections is not unexpected in areas where *Aedes albopictus* mosquitoes are established and at a time when environmental conditions are favouring mosquito abundance and activity. This is the second time that Italy is facing an outbreak of autochthonous chikungunya, following an outbreak in the Emilia-Romagna region in 2007. Within the European Union, apart from Italy, only France reported outbreaks of autochthonous cases in the past, i.e. in 2010, 2014 and 2017.

Autochthonous chikungunya transmission is estimated to have started in Anzio in early-/mid-June 2017 or earlier. Subsequently, autochthonous transmission was detected in Rome and Latina, and more recently in Guardavalle Marina. The likelihood of further spread within Italy is still moderate, with suitable but less favourable conditions for vector activity in the coming weeks. In the areas already affected, it is likely that more cases will be identified in the near future.

Environmental conditions for mosquito breeding and activity in Europe are expected to become less favourable in the coming weeks. Therefore, there is only a low likelihood that the virus will be introduced to other EU countries with present and active *Aedes albopictus* populations and lead to subsequent local transmission.

Early detection of imported chikungunya cases at the start of the season of high mosquito activity is critical to prevent establishment of local transmission if the virus was introduced by a viraemic traveller to an area where *Aedes albopictus* is established. This relies on increased awareness among clinicians and travellers returning from areas with chikungunya transmission, combined with adequate laboratory capacity.

The detection of an autochthonous case should trigger epidemiological and entomological investigations to assess the potential of onward transmission and guide vector control measures aimed at lowering mosquito population density. Member States should consider reporting all confirmed cases of chikungunya who travelled to Italy in the two weeks before the onset of symptoms to the Italian health authorities in order to help identify possible additional transmission foci.

In addition to coordinated vector surveillance and vector control activities, community sensitisation around transmission foci is important. It is important to inform people of the need for personal protection measures against mosquito bites and to engage local communities in the elimination of mosquito breeding sites. Personal protective measures to reduce the risk of mosquito bites include the use of mosquito repellent in accordance with the instructions on the product label, wearing long-sleeved shirts and long trousers – especially during the daytime when *Aedes albopictus* mosquitoes are most active – sleeping and resting in screened or air-conditioned rooms, and using mosquito nets for beds.

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Member States should consider the following measures to prevent the transmission of chikungunya through substances of human origin (SoHO):

- Excluding donations from travellers returning from affected areas in Italy.
- Screening donors through nucleic acid testing (NAT) in affected areas.
- Temporarily interrupting donations in affected areas in the absence of validated and authorised NAT for the screening of donors.
- Deferring donors diagnosed with chikungunya for at least four weeks after the resolution of symptoms, as suggested by data available on viraemia during and after chikungunya infection.
- Applying effective pathogen inactivation for the apheresis collection of platelets and plasma in affected areas.
- Reminding donors to report symptoms after donation in areas infested by *Aedes albopictus*
- Consulting a transplant infectious disease expert before considering organ donation from donors infected with chikungunya virus.

The SoHO safety measures should be applied at a geographical level that takes into account the estimated extent of transmission and the daytime movements of the local population from the affected area. Currently, the municipalities of Anzio, Guardavalle Marina, Latina and Rome are considered to be affected areas.

Source and date of request

ECDC internal decision, 2 October 2017.

Public health issue

In the context of the detection of a cluster of autochthonous chikungunya cases in Calabria, southern Italy, this assessment aims to address the likelihood of further local and international spread, as well as the public health impact of the event.

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All experts have submitted declarations of interest. A review of these declarations did not reveal any conflict of interest.

Experts from WHO reviewed this risk assessment. However, the views expressed in this document do not necessarily represent the views of WHO.

Disease background information

Chikungunya is an *Aedes* mosquito-borne viral disease widely distributed in tropical regions of Africa, southeast Asia, the Indian subcontinent, the Pacific region. It has been present in the Americas since 2013. The disease is mainly spread by the bite of *Aedes* mosquitoes, primarily *Aedes aegypti* and *Aedes albopictus*, two species that are active during the day and can transmit other mosquito-borne viruses such as dengue and Zika. Autochthonous chikungunya outbreaks in the European Union were reported in 2007 (Emilia Romagna region, Italy) and in 2010, 2014 and 2017 in the Var and Hérault departments, France [1,2] (Annex 1).

The disease usually results in high fever, myalgia, skin rash and noticeable arthralgia. Over 75% of the infections are symptomatic [3-6]. In humans, the viral load in the blood can be very high at the beginning of the infection and lasts 5–6 days after onset of fever [7]. Chronic arthralgia may persist for weeks or months, causing a significant disease burden in the affected communities [8-10]. The medical treatment costs and productivity losses associated with a large chikungunya outbreak represent a noticeable economic burden [11]. Complications are rare [12]. No specific treatment or licenced vaccine is currently available [13].

Transmission of chikungunya virus infection through transfusion and transplantation has not been reported in humans. Chikungunya virus was detected in asymptomatic blood donors in Puerto Rico in 2014 [14]. Viraemic blood donations were identified in previous outbreaks in Thailand [15], La Réunion [16] and Italy [17]. Infectious virus and viral RNA were found in the cornea and sclera of deceased donors in La Réunion [18]. Therefore, the risk of chikungunya transmission through blood, cells, tissues and organs cannot be excluded.

ECDC's chikungunya web page [19] and chikungunya factsheet [20] provide information on chikungunya disease. ECDC published a rapid risk assessment on a cluster of autochthonous chikungunya cases in France on 23 August 2017 [2] and a rapid risk assessment on a cluster of autochthonous chikungunya cases in Italy on 14 September 2017 [21]. ECDC monitors global outbreaks of chikungunya, dengue and Zika on a monthly basis. Updates are available in the weekly ECDC Communicable Disease Threats Report [22]. Information on *Aedes albopictus* vectors can be found in the factsheet for experts [20]. The latest information on vector distribution is available in ECDC's mosquito maps, which were last updated in September 2017 (Annex 2) [23]. Background information and advice on chikungunya prevention and control are available in ECDC's Communication toolkit on chikungunya: how to prevent and control chikungunya? [24].

Event background information

On 7 September 2017, the Italian Ministry of Health reported through the Early Warning and Response System (EWRS) a cluster of three cases of chikungunya in the city of Anzio, located in the coastal area of Lazio region, Rome Province, central Italy. On 13 September, six cases of chikungunya were reported in the capital city of Rome, Lazio.

As of 4 October, Italy has reported 239 chikungunya cases in the Lazio region (146 confirmed and 93 probable) and six confirmed autochthonous cases among 55 reported cases in the city of Guardavalle Marina, Calabria region. Several probable and confirmed cases were reported in other regions of Italy (i.e. Emilia-Romagna, Marche) [25] and other EU Member States (France and Germany). All were epidemiologically linked to Anzio, Rome or Guardavalle Marina. This brings the number of reported cases in Italy to 298 cases.

The Lazio region has an estimated 5.8 million inhabitants, with 4.3 million in the Metropolitan City of Rome, 125 000 inhabitants in Latina and 55 000 in Anzio. Guardavalle Marina is a town of less than 5 000 inhabitants, 660 km south of Rome.

The virus circulating in Anzio, Italy, belongs to the East/Central/South African (ECSA) lineage and shows on a limited analysed amplicon fragment (507 bp, sequence available in GenBank) 100% homology with two strains from Pakistan and India from 2016 [26]. The isolated virus does not carry the E1-A226V mutation which is known to facilitate the transmission by *Aedes albopictus*, as reported in the Indian Ocean in 2005–2006 [27]. Sequencing of the strain circulating in Calabria is ongoing.

On 11 August 2017, France reported through EWRS an outbreak of autochthonous chikungunya cases in the city of Cannet-des-Maures, Var department, southern France. As of 3 October, France has reported 17 cases (13 confirmed, three probable and one suspected) distributed in two clusters: 11 cases in Cannet-des-Maures (eight confirmed, two probable and one suspected), with date of onset between 28 July and 30 August, and six cases in Taradeau (five confirmed and one probable), with date of onset between 26 August and 9 September [28]. Cannet-des-Maures and Taradeau are ten kilometres apart, and the two clusters are considered epidemiologically linked. The virus circulating in France is different from the one identified in the Lazio region in Italy. It belongs to an ECSA sub-lineage that includes isolates from the Central African region (e.g. Gabon, Republic of Congo) and carries an adaptive E1-A226V mutation [29].

Figure 1. Distribution of chikungunya autochthonous cases in Italy, July to 3 October 2017

The Italian authorities are defining a probable case as a person presenting with symptoms compatible with chikungunya and testing positive for IgM, and a confirmed case as a person presenting with symptoms and testing positive by RT-PCR or neutralisation test.

In the Lazio region, Rome province, *Aedes albopictus* was first detected in 1997 and was considered to have become established in subsequent years [30]. In the coastal central region of Italy, *Aedes albopictus* is considered to be active all year long, with peaks in activity during the summer and autumn [30,31,36].

The Italian authorities are conducting epidemiological and entomological investigations around the clusters in Anzio, Latina, Rome and Guardavalle Marina. Italy implemented a number of measures, which are outlined below.

Epidemiological investigations to identify additional cases, enhancing surveillance activities:

- Case finding in the community and in healthcare settings by general practitioners, paediatricians, in emergency rooms and hospitals admissions.
- Rapid reporting of suspected cases and retrospective investigation to identify past infections.
- Entomological investigations around potential places of exposure.

In the Lazio region, vector control activities were performed by aerial spraying with pyrethroid insecticides to quickly reduce of the adult mosquito population and by residual etofenprox-based insecticides which were applied to the vegetation to target resting mosquitoes. Measures against mosquito larvae involved products based on mixed *Bacillus thuringiensis* var. *israelensis* and *Bacillus sphaericus* in street drains where water was present. Insecticide treatments were targeted at public areas (streets and parks) and private houses with gardens if possible, as many summer homes in Anzio sit vacant during off-season months. One course of insecticides was administered on 7 September 2017 in the area where the first three cases were recorded. Heavy rainfall in the following days interrupted treatment activities, preventing further mosquito control action. From 12 to 18 September 2017, adulticide and larvicide treatments were administered in public and private areas, whereas larvicide treatment was only administered throughout the municipalities' public areas. Pyrethroid insecticides were used for adult mosquitoes, and diflubenzuron (a larvicide) was used in Guardavalle Marina. More insecticides were applied in the following days after the authorities received further reports of infected patients. Control activities are still ongoing.

The mosquito monitoring guidelines used were those indicated in the national plan for surveillance and control of arboviruses by the Italian Ministry of Health (2016). On 28 September 2017, the Ministry of Health issued new recommendations to strengthen surveillance and control activities at the national level, including disinfestation at ports and airports.

Blood safety preventive measures

- Temporary interruption of donations in affected areas (Anzio and in the affected districts of Rome) in absence of validated and authorised acid testing (NAT) for the screening of donors. Considering the potential impact on the blood supply and the limited number of cases, a five-day quarantine of blood components (red blood cells) collected in Latina was applied instead of interrupting donations.
- Collection of plasma for fractionation is being maintained.
- A five-day quarantine for blood components (red blood cells) collected in the non-affected areas of Rome as a precautionary measure due to the high mobility of the Roman population.
- Deferring donors diagnosed with chikungunya for at least four weeks after the resolution of symptoms.
- Applying effective pathogen inactivation for the apheresis collection of platelets and plasma in affected areas.
- Reminding donors to report symptoms after donation in areas infested by *Aedes albopictus*.
- Application of a 28-day deferral in relation to donor residents in the municipalities of Anzio, Rome and Guardavalle Marina.

Preventive blood safety measures will be adapted according to the results of epidemiological investigations. Emergency risk communication to the population about chikungunya and information on protection against mosquito bites is ongoing. Ministry of Health's website features dedicated pages about chikungunya. In addition, information and guidelines for healthcare practitioners on how to manage patients were disseminated.

Travel data

In 2016, according to the International Air Transport Association, 13.3 million people travelled by air from EU Member States to Rome's two international airports, Ciampino and Fiumicino. Most passengers to Rome originated in Italy (31% of passengers), Spain (12%), the United Kingdom (11%), France (9.4%) and Germany (8.3%) (Annex 3). In 2016, according to the International Air Transport Association, 1.1 million people travelled by air from EU Member States to Lamezia airport, Calabria. Most passengers to Lamezia originated in Italy (82%), Germany (9.0%) and the United Kingdom (2.8%).

ECDC threat assessment for the EU

Both France and Italy reported autochthonous transmission of chikungunya virus during the summer of 2017. The report of a cluster of autochthonous chikungunya cases in an area of Europe where *Aedes albopictus* is established is not unexpected during summer and autumn months when environmental conditions are favourable for increased mosquito abundance and activity.

The primary viraemic case who introduced the virus to Italy has not been identified. Based on a limited sequence analysis, the viral strain circulating in Anzio shows homology with two strains which are currently causing outbreaks in Pakistan and India. Therefore, it could be hypothesised that the primary case has an epidemiological link with southern Asia.

Anzio and Guardavalle Marina are holiday resorts. Anzio is less than one hour away from Rome, with extensive travel between the two cities. During the summer holidays the population density increases in both resort towns. Viraemic individuals exposed in August 2017 in Anzio are likely to have travelled to other areas, possibly resulting in new introductions in receptive areas and challenging the implementation of control measures. As summer houses sit vacant after the holiday season ends in mid-September, comprehensive vector control activities in Anzio are difficult to implement. In Calabria, there is currently no evidence of other cases of chikungunya outside of Guardavalle Marina municipality.

Aedes albopictus has been confirmed as a competent vector for both chikungunya virus genotypes (ECSA and Asian) [33-35]. Population dynamics of *Aedes albopictus* are mainly driven by temperature, daylight duration (which influences the survival of adults and the development of larvae) and rainfall. Rainfall increases the number of breeding sites, both natural (small bodies of water) and man-made (e.g. flowerpot plates, old tyres, buckets, rain barrels, gutters) [36].

Aedes albopictus mosquitoes are active all year long in tropical and subtropical regions. In most temperate areas, mosquitoes overwinter in the egg stage, with no adult mosquito activity during winter months. However, in central Italy, the adult *Aedes albopictus* mosquitoes are showing signs of cold acclimation and may remain active throughout the winter [30,31,36]. In 2012, a study of *Aedes albopictus* population dynamics in metropolitan and suburban/rural sites in Rome showed bi-modal seasonal dynamics, with a first peak of abundance in August and a second in October, due to heavy rains in the preceding weeks in association with permissive temperatures [30]. In Calabria, the peak of abundance is from July to early October [37]. This highlights that transmission might continue in the coming weeks until temperatures drops below permissive levels. Effective vector control activities are paramount to reduce vector density and activity and thus limit further transmission in affected areas.

Aedes albopictus is an outdoor mosquito that bites aggressively during the day, with feeding peaks in the early morning and late afternoon. Reports have found that *Aedes albopictus* mosquitoes have become partially endophilic and may bite indoors [35,38]. A study in Rome found that local *Aedes albopictus* mosquito populations

could rest indoors after a blood meal, resulting in the reduced effectiveness of outdoor vector control activities [39].

Aedes albopictus mosquitoes have the ability to breed in natural and artificial habitats. The availability of anthropogenic breeding sites (e.g. flowerpot plates or water containers) is considered a key factor for the preservation of *Aedes albopictus* populations during hot and dry periods, as reported in the French Riviera in southern France [36]. In addition, in the Rome area, the high abundance of adult *Aedes albopictus* has been found to be significantly associated with the level of urbanisation in metropolitan and suburban or rural areas, and around small green islands that provide many resting and breeding sites [30]. This would suggest that urban areas are not exempted from chikungunya transmission.

The A226V mutation in the envelope protein E1 of the ECSA genotype was first observed in the outbreak in La Réunion in 2005, and later in the Emilia-Romagna region in Italy in 2007 and the Hérault and Var departments in France in 2014 and 2017, respectively. The acquisition of an A226V mutation in the envelope protein E1 of the ECSA genotype has been recognised to increase the transmissibility of the virus through *Aedes albopictus* mosquito species [27,40]. The absence of this mutation in the strain associated with the current outbreak in Italy could result in a lower competency of *Aedes albopictus* mosquitoes to the virus. However, the transmissibility of the virus in this outbreak has been high, as the outbreak has been ongoing for three months, with new cases reported every week and additional transmission foci observed in two different regions in the country. This underlines that the absence of the mutation does not prevent the occurrence of multi-foci outbreaks, as long as the environmental conditions are suitable for the transmission of the virus.

Sequencing of the strain involved in the Calabria cluster will provide evidence on whether the cluster is related to the Anzio, Latina and Rome clusters.

An *Aedes albopictus* mosquito can usually transmit chikungunya virus to a new person 2 to 14 days after having bitten a viraemic patient (known as the 'extrinsic incubation period') [41-44]. The extrinsic incubation period of chikungunya virus in *Aedes albopictus* can be shortened by warmer temperatures, particularly when the mutated A226V ECSA strain is involved [27,45]. The incubation period in a person bitten by an infective mosquito is two to four days on average, ranging from one to twelve days. As the date of onset of the first reported local case was 25 June 2017, it is expected that the virus was introduced around early-/mid-June 2017 or earlier. Several mosquito generations have been involved in the transmission.

Vertical transmission in *Aedes aegypti* populations has been suspected for sustaining chikungunya transmission. However, there is only very limited evidence of vertical transmission of chikungunya in *Aedes albopictus* populations from the Indian Ocean or from Italy [46,47]. In addition, field observations conducted during the spring of 2008 in Emilia-Romagna, Italy, showed no evidence of the presence of infected overwintering progeny produced by *Aedes albopictus* females infected during the 2007 outbreak [48].

This is the first known transmission of chikungunya in central and southern Italy and therefore, in the absence of herd immunity, most of the inhabitants should be considered as susceptible to chikungunya virus disease. The likelihood of further spread within Italy is still moderate, with suitable but less favourable conditions for vector activity in the coming weeks. In the areas already affected, more cases can be expected to be identified in the near future. There is a low likelihood of introduction of the virus to, and subsequent local transmission in, other EU countries where *Aedes albopictus* is present and active.

The number of cases currently reported by Italy remains very low compared with the number of cases occurring in some subtropical and tropical countries. The likelihood of introduction of the virus to continental EU countries through viraemic travellers returning from endemic subtropical and tropical countries is high. However, the establishment of local transmission following the introduction to an area where *Aedes albopictus* is present, is considered low in continental EU countries at this time of the year. Therefore, the current outbreak in Italy does not significantly increase the overall risk of introduction and further spread of chikungunya to other EU countries.

The pathogenicity of the virus and asymptomatic viraemia in blood donors suggest that chikungunya transmission via substances of human origin (SoHO) is possible.

Disclaimer

ECDC issues this risk assessment document on the basis of an internal decision in accordance with Article 10 of Decision No 1082/13/EC and Article 7(1) of Regulation (EC) No 851/2004 establishing a European centre for disease prevention and control. In the framework of ECDC's mandate, the specific purpose of an ECDC risk assessment is to present different options on a certain matter with their respective advantages and disadvantages. The responsibility on the choice of which option to pursue and which actions to take, including the adoption of mandatory rules or guidelines, lies exclusively with the EU/EEA Member States. In its activities, ECDC strives to ensure its independence, high scientific quality, transparency and efficiency.

This report was written under the coordination of an Internal Response Team at the European Centre for Disease Prevention and Control. All data published in this risk assessment are correct to the best of our knowledge on 5 October 2017. Maps and figures published do not represent a statement on the part of ECDC or its partners on the legal or border status of the countries and territories shown.

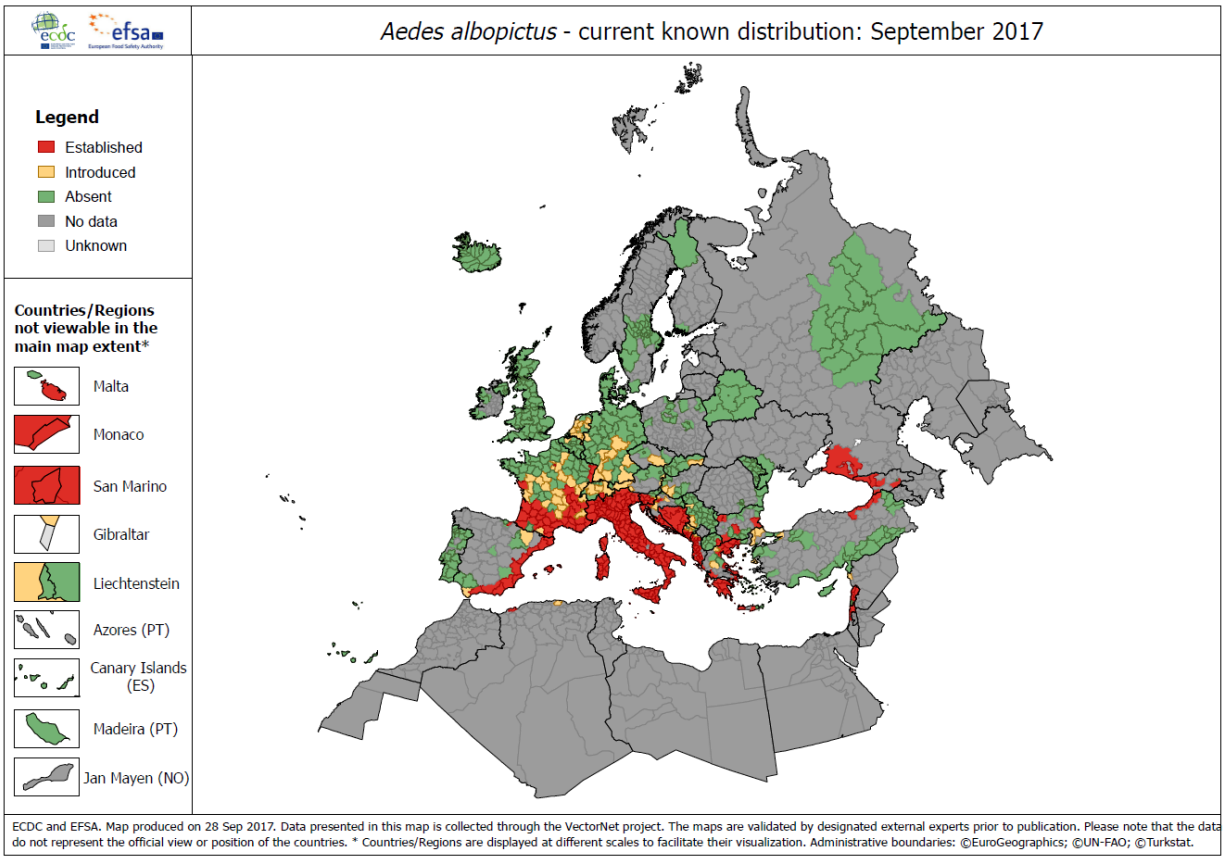
Annex 1. Autochthonous transmission of dengue and chikungunya in Europe

Year	municipalities	Typology of areas of transmission	Number of cases	Period	Likely origin of the strain	CHIKV genotype	Reference
2007	Italy, region of Emilia Romagna, main transmission areas in Castiglione di Cervia and Castiglione di Ravenna villages.	Rural villages	≈ 330 suspected and confirmed cases	July–September	India	ECSA E1-A226V CHIKV strain (with mutation)	[40,49]
2010	France, Var department, Fréjus city	Urban/sub-urban	Two cases	September	India	ECSA E1-A226 CHIKV strain (without mutation)	[33,50]
2014	France, Hérault department, Montpellier	Urban/sub-urban	Eleven cases	September–October	Cameroon	ECSA E1-A226V CHIKV strain (with mutation)	[51]
2017	France, Var department, Le Cannet-les-Maures	Small town in rural area	As of 3 October, 17 cases: eleven in Cannet-des-Maures and six in Taradeau	July–October	Central Africa	ECSA E1-A226V CHIKV strain (with mutation)	[29,52]
2017	Italy, Lazio region, Anzio, Latina and Rome and Calabria region (Guardavalle marina)	Urban/sub-urban with commuting	As of 4 October, 239 cases in the Lazio region and six cases in Guardavalle Marina.	August–October	In Lazio: Asia (India/Pakistan) In Calabria: ongoing	In Lazio: ECSA E1-A226 CHIKV strain (without mutation) In Calabria: ongoing	[26,53]

CHIKV: Chikungunya virus

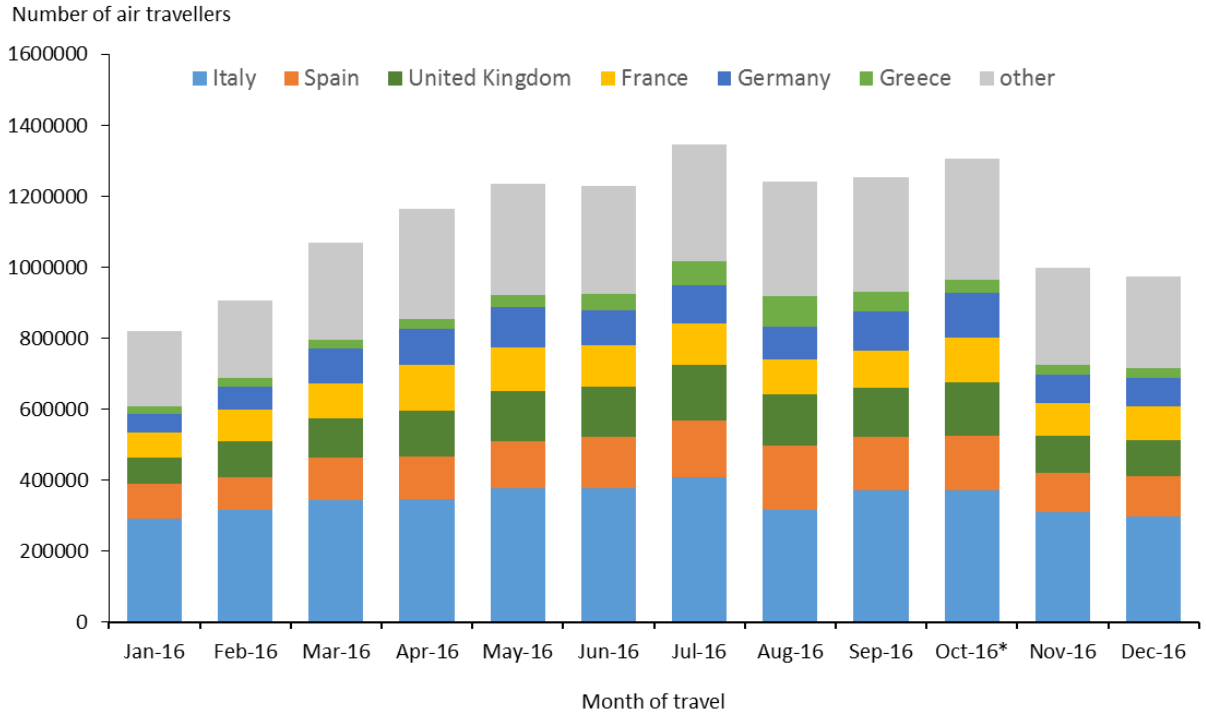
ECSA: East/Central/South African CHIKV lineage.

Annex 2. Current known distribution of *Aedes albopictus* in the EU and neighbouring countries, September 2017



Aedes aegypti, the main vector of chikungunya, is present around the Black Sea and in Madeira [54].

Annex 3. Number of air travellers from EU countries to Rome by month in 2016



** Data for Ciampino Airport are from October 2015.*

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