Position Statement

September 2025

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Usutu Virus

Background

Usutu virus (USUV) is an emerging arbovirus of the *Flaviviridae* family and a member of the Japanese encephalitis virus (JEV) serocomplex, which also includes West Nile virus (WNV), Murray Valley encephalitis virus, and Japanese encephalitis virus. USUV maintains a natural enzootic cycle between ornithophilic mosquitoes – primarily *Culex* species in Europe – and avian hosts, with humans and other mammals, including horses and rodents, considered incidental or dead-end hosts.

First isolated in South Africa in 1959 from *Culex* mosquitoes, USUV was not detected outside of Africa until 2001, when it was identified as the cause of significant avian mortality among Eurasian blackbirds in Austria. Since 2001, the virus has become established in numerous European countries, including Belgium, Germany, the Netherlands, Italy, and more recently the UK (Folly et al, 2020).

Human infections with USUV were first reported in Europe in 2009, in Italy, where two immunocompromised patients developed meningoencephalitis, with one also experiencing fulminant hepatitis (Pecorari et al, 2009; Cavrini et al, 2009). Sporadic human cases have continued to be reported across Europe, often in association with neurological symptoms, particularly among immunocompromised individuals.

Despite genetic and ecological similarities with WNV, USUV appears to exhibit lower overall pathogenicity in humans. It has been implicated in a range of clinical presentations, from mild febrile illness with rash to severe neuroinvasive disease. Documented symptoms include headache, fever, rash, jaundice, hand tremor, nuchal rigidity, and hyperreflexia (Cadar and Simonin, 2022).

Although human cases remain relatively rare, the expanding geographic range of USUV in Europe, coupled with its demonstrated neurovirulence and capacity to persist in endemic mosquito populations, raises concerns about its public health impact and potential relevance to transfusion safety.

Epidemiology, pathogenesis, infection dynamics and clinical characteristics relevant to the safety of substances of human origin (SoHO)

As of the end of 2023, over 230 confirmed human cases of USUV infection have been reported globally, with the majority occurring in Europe – particularly in Italy (approximately 60%) and Austria (27%) (Chen et al, 2024). Notably, over 85% of these cases have occurred between June and September, reflecting the seasonality of mosquito-borne virus transmission.

USUV is assumed to behave similarly to WNV in terms of infection dynamics but detailed studies are still lacking. Viraemia thought to be typically short-lived, occurring within 2 to 14 days of symptom onset. Prolonged RNA detection in symptomatic individuals has been documented in whole blood; viral RNA has been detected in blood 40 days post onset of illness with central nervous system involvement. (Pacenti et al, 2019).

Human infection typically presents with an incubation period of 2 to 14 days. USUV RNA can be detected in plasma or cerebrospinal fluid during the acute phase, and IgM antibodies generally appear within 5 days of symptom onset, persisting in serum for several months.

USUV in the EU/EAA

The primary European vector is *Culex pipiens*, although other species, including *Aedes* mosquitoes, may also contribute to transmission. Transovarial transmission in *Culex* mosquitoes under temperate conditions has been suggested in UK-based field studies, supporting local overwintering and persistence of the virus (Schilling et al, 2025).

The virus has been associated with periodic epizootics in various European countries. Sporadic human cases were initially reported in Germany (Allering et al, 2012) and Croatia (Vilibic-Cavlek et al, 2014), with increasing numbers of cases identified in subsequent years (Cle et al, 2019). During a period of avian epizootic activity in 2018, seven of 9,352 blood donations in the Netherlands were found to be USUV RNA positive (Zaaijer et al, 2019).

Importantly for transfusion safety, USUV is known to cross-react in donor screening assays designed for WNV. In Austria, six of seven blood donations initially reactive in a WNV RNA screening assay in 2017 were subsequently confirmed to be USUV infections (Bakonyi et al, 2017). More recently, USUV RNA was detected in a blood donor in Piedmont, Italy during routine WNV screening (Lupia et al, 2022).

USUV in the UK

USUV was first identified in the UK in August 2020 in a small number of wild birds. Phylogenetic analysis indicated that the virus belonged to the African 3.2 lineage, which is also known to circulate in Belgium and the Netherlands. This detection prompted a review of the existing UK Human Animal Infections and Risk Surveillance (HAIRS) group risk assessment.

The most recent HAIRS assessment concluded that the probability of human USUV infection in the UK remains low, with a low to moderate potential impact for immunocompromised individuals.

Risk mitigation

(as applicable, e.g. measures adopted by UK blood, haematopoietic stem cells and tissue establishments, if any; availability of efficacious preventative measures, prophylaxis or treatment)

To date, there have been no confirmed cases of transfusion-transmitted USUV infection. Blood donors returning from high vector-burden areas of Europe must comply with the requirements for WNV.

Due to the shared vectors, epidemiology and areas of ongoing transmission activity between WNV and USUV, current safety measures for WNV offer indirect overlapping cover through deferral or testing for virus RNA. The blood donor screening tests in use by UK blood services target the various viruses in the same family and USUV infections in blood donors have been identified through this route.

Presently, there is no justification to introduce a specific entry for USUV for donor assessment.

Other relevant information

Information on international and UK-based activity of USUV is monitored through JPAC emerging infection surveillance activity which also includes reports from the UK Health Security Agency (UKHSA), the European Centre for Disease Prevention and Control (ECDC), and relevant publications including reports from the HAIRS group.

Current guidance regarding countries affected by vector-borne viruses, including any applicable time limits for donor deferral, is available on the JPAC website, within the Geographical Disease Risk Index (GDRI) and any associated Change Notifications.

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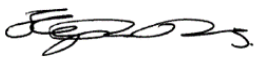

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