

**Recommendation of the ZKBS on the risk assessment of
Severe fever with thrombocytopenia syndrome phlebovirus (SFTSV)
as donor or recipient organism according to Article 5 paragraph 1 GenTSV**

General

The *Severe fever with thrombocytopenia syndrome phlebovirus* (SFTSV; synonyms: Huaiyangshan virus, HYSV; Henan fever virus, HNFV) belongs within the family of *Phenuiviridae* (order *Bunyvirales*) to the genus *Phlebovirus*. The genome of SFTSV consists of three ssRNA segments of negative polarity with a total length of approx. 11.5 kb [1].

In 2009, the inhabitants of rural areas in central and northeastern China experienced a high incidence of a novel disease, the so-called *Severe fever with thrombocytopenia syndrome* (SFTS) [1]. Cause of this disease is an infection with SFTSV [2 - 4]. The clinical picture of SFTS includes fever, head, muscle and joint pain, diarrhoea, leukocytopenia, thrombocytopenia, bradycardia, proteinuria and hematuria. In severe courses of disease, gastrointestinal and pulmonary haemorrhage and multi-organ failure may also occur; in rare cases, pneumonia is also described [5]. However, asymptomatic infections also occur [2; 6; 7]. The case fatality rate of the disease is 6 - 33 % [1; 2; 5; 6; 8 - 10]. There are indications that an individually different genetic susceptibility for SFTSV influences the severity of the infection [11]. Although the efficacy of ribavirin against SFTSV is proven *in vitro*, the treatment of SFTS patients with ribavirin has no effect on the course of the disease. [12].

Since its first appearance, SFTSV has continued to expand. Meanwhile, the distribution area of SFTSV also extends to North and South Korea as well as Japan [2; 10].

SFTSV has a broad host range. The virus has been detected in a wide range of domestic and wild animals such as goats, sheep, chickens, cattle, dogs, mice, rats and hedgehogs, with domestic animals in particular showing a high prevalence [7; 10; 13]. The infected animals show no or only mild symptoms of the disease and may serve as amplifying hosts or reservoir for the virus.

The natural route of transmission of SFTSV is not yet fully understood. Most representatives of the genus *Phlebovirus* are transmitted by sandflies, while the *Uukuniemi virus* is transmitted by ticks. SFTSV can probably also be transmitted to humans by ticks, since viral RNA could be detected in the ticks *Haemaphysalis longicornis* and *Rhipicephalus microplus* with low frequency (approx. 0.2 - 5 % and 0.6 %, respectively) [1; 13; 14]. In addition, some of the patients reported tick bites in close temporal relation to the disease [7; 9; 15]. Animal experiments have also shown that SFTSV-infected ticks transmit the virus to mice during blood meal [13]. Whether other blood-sucking arthropods also play a role in the transmission of SFTSV is still unclear. However, viral RNA was also found in mites and horse flies parasitising on mice and goats, while mosquito species from endemic areas were SFTSV-negative [1; 13]. In addition, there are a number of reports of a human-to-human transmission of SFTSV. The literature

describes a number of cases (family members, hospital staff) in which the secondary patients were not bitten by ticks during the period in question but had contact with the blood or bloody vomitus of the index patients [2 - 6; 8; 15 - 17]. It can therefore be assumed that the virus can also be transmitted via direct contact with infected persons. Transmission by contact with the blood of infected animals is also under discussion.

In Technical Rules for Biological Agents (TRBA) 462 "Classification of viruses into risk groups", SFTSV has so far been assigned to **risk group 3** [18].

Recommendation

According to Article 5 paragraph 1 GenTSV in conjunction with the criteria in Annex I GenTSV, *Severe fever with thrombocytopenia syndrome phlebovirus* (SFTSV) is assigned to **risk group 4** as donor and recipient organism for genetic engineering operations.

Reasoning

Severe fever with thrombocytopenia syndrome phlebovirus (SFTSV) has a broad host range that includes ticks, various mammalian? species and humans. The virus can cause a serious disease in humans, which can be fatal in up to a third of cases. Vaccination or antiviral therapy is not available. SFTSV is probably transmitted by ticks. The virus can also be transmitted through direct contact with infected individuals and possibly also infected domestic and wild animals.

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