Keystone virus was discovered in Keystone, Florida, in 1964. The virus occurs in coastal pine forests and freshwater swamps in the mid-Atlantic and southeastern regions of the United States. The virus is not known to be of public health importance. No symptomatic infections have been reported in people. Important reservoirs for the virus include cotton rats, eastern grey squirrels, and cottontail rabbits.

_Aedes atlanticus_ and _Aedes atlanticus/tormentor_ are the primary mosquito vectors. Transmission of the virus from the mosquito vector to its offspring (transovarian transmission) is critical to maintenance of Keystone virus in the environment.