



New Development: SERION ELISA *classic* Dengue Virus superior IgM

Dear Ladies and Gentlemen,

With our SERION ELISA *classic* product line we provide a wide range of diagnostic tests for infectious serology. We are very happy to announce that the panel of tropical infectious diseases is now complemented by the new SERION ELISA *classic* Dengue Virus superior IgM test system.

Dengue fever is currently one of the most important arboviral causes of infectious diseases and deaths in humans. The virus is transmitted to humans by the mosquito vectors *Aedes aegypti* and *Aedes albopictus*. These mosquitoes are also vectors of Chikungunya Virus, Yellow Fever Virus and Zika Virus. Around 3.9 billion people in approximately 129 countries reside in dengue endemic risk areas. According to the World Health Organization (WHO), up to 390 million cases of dengue fever occur worldwide each year ^[1,2].

For laboratory confirmation, direct pathogen detection (NS1 antigen detection or PCR) is recommended between day 1 and day 5 after the onset of symptoms. Due to the immune response and pathogen clearance, the diagnostic efficiency of these methods decreases significantly after day 4. Subsequently, serology is the method of choice for laboratory diagnostics of a Dengue Virus infection. IgM antibodies are detectable in 80% of all infections by day 5, 99% by day 10 and peak after 2 weeks and then decline over 2 - 3 months. Anti-dengue IgG may be detected at low levels by the end of the first week of illness and persist several months or even for life ^[1,2].

Especially in areas where other members of the family *Flaviviridae* (such as Zika Virus, Yellow Fever Virus (-vaccine strain or natural infection-), West Nile Virus, Saint Louis Encephalitis Virus, Japanese Encephalitis Virus) co-circulate, cross-reactivities should be taken into consideration because of the high homology between this group of viruses ^[1,2].

To support the diagnosis of a Dengue Virus infection or to carry out epidemiological studies, Institut Virion/Serion GmbH offers already since 2011 SERION ELISA *classic* Dengue Virus IgG and IgM immunoassays for the qualitative and quantitative detection of human antibodies in serum or plasma against dengue viruses (DEN 1 - 4).

While the SERION ELISA *classic* Dengue Virus IgM test utilizes inactivated virus lysate for a sensitive antibody detection, recombinantly expressed species-specific peptides from the envelope protein are the fundamental component for antibody determination with SERION ELISA *classic* Dengue Virus IgG to reduce cross reactions.

Due to the rapidly emerging infections caused by flaviviruses the requirements for the specificity of Anti-Dengue Virus IgM detection systems are increasing, especially in endemic regions.

SERION ELISA *classic* Dengue Virus superior IgM

Therefore we are more than happy to offer the new SERION ELISA *classic* Dengue Virus superior IgM for the detection of qualitative and quantitative human IgM antibodies in serum or plasma against dengue viruses (DEN 1 - 4). The test allows for the specific detection of acute Dengue Virus infections also in the context of differential diagnosis of diseases caused by flaviviruses and is particularly recommended for regions with a high prevalence of flaviviruses (West Nile Virus, Japanese Encephalitis Virus, Yellow Fever Virus).

Analogous to the SERION ELISA *classic* Dengue Virus IgM test, the SERION ELISA *classic* Dengue Virus superior IgM is based on a lysate of inactivated Dengue Viruses. By using a modified and therefore more stringent special dilution buffer DILBS4 included in the kit, binding of cross-reactive antibodies as well as antibodies with low activity is prevented.

To analyze the specificity, an internal study was recently conducted using a total of 139 clinically negative sera collected in regions where other flaviviruses are endemic. This included 80 samples of pregnant women from Brazil, 34 Zika Virus positive and 25 West Nile Virus positive sera, collected in the period from 2016 to 2019. Using the SERION ELISA *classic* Dengue Virus superior IgM test, only 8 sera were evaluated positive. In comparison, with the SERION ELISA *classic* Dengue Virus IgM as well as with a reference ELISA more sera were rated positive (20 and 16 sera, respectively).

Thus, a high specificity of 93.8% determined against negative clinical evaluation could be shown for the SERION ELISA *classic* Dengue superior IgM using a serum panel from areas with high flavivirus infection rates. The reference ELISA and the SERION ELISA *classic* Dengue Virus IgM have somewhat lower specificities of 88.0 and 84.0%, respectively (Table 1 and 2).

Table 1: Result distribution of immunoassays among a panel of samples from regions with high flavivirus infection rates.

	Clinically negative serum samples			
	positive	borderline	negative	total
SERION ELISA <i>classic</i> Dengue Virus superior IgM	8	4	122	134
SERION ELISA <i>classic</i> Dengue Virus IgM	20	14	105	139
Reference ELISA	16	6	117	139

Table 2: Specificities in comparison to clinical symptoms among a panel of samples from regions with high flavivirus infection rates.

	Specificity against clinical symptoms (negative)
SERION ELISA <i>classic</i> Dengue Virus superior IgM	93.8 %
SERION ELISA <i>classic</i> Dengue Virus IgM	84.0 %
Reference ELISA	88.0 %

The use of the modified dilution buffer included in the SERION ELISA *classic* Dengue Virus superior IgM kit of course may have impact on the detection of weakly binding or low concentrated anti-Dengue Virus-specific IgM antibodies. In order to determine whether high sensitivity is still guaranteed, an internal study was carried out with a total of 243 sera from Colombian patients with suspected infection. A sensitivity of 91.5% was determined for the SERION ELISA *classic* Dengue Virus superior IgM compared to the reference ELISA and a somewhat higher sensitivity of 94.7% for the SERION ELISA *classic* Dengue Virus IgM (see Table 3).

Table 3: Sensitivities in comparison to the reference ELISA among a panel of samples from patients with suspected infection, collected in Colombia.

	Sensitivity against the Reference ELISA
SERION ELISA <i>classic</i> Dengue Virus superior IgM	91.5 %
SERION ELISA <i>classic</i> Dengue Virus IgM	94.7 %

With the launch of our new SERION ELISA *classic* Dengue superior IgM you now have the possibility to choose between two anti-Dengue Virus IgM tests with high diagnostic efficiencies. If a very sensitive and early detection of anti-Dengue Virus IgM antibodies is required, we recommend the use of the SERION ELISA *classic* Dengue Virus IgM. For regions where other flaviviruses are endemic and therefore a high demand on the specificity of the test system exists, we recommend the use of the SERION ELISA *classic* Dengue Virus superior IgM test.

Please find attached more detailed information about our new SERION ELISA *classic* Dengue Virus superior IgM test. If you have any questions regarding our products, please do not hesitate to contact us.

**Best regards,
Institut Virion\Serion GmbH**

[1] 2018_WHO Weekly epidemiological record
[2] 2016_Dengue Guideline in the region of the americas