# Elecsys Zika IgG

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| REF | Σ | SYSTEM |
|---|---|---|
| | | **cobas e** 411 |
| **08176078** 119 | 100 | **cobas e** 601 |
| | | **cobas e** 602 |

**English**

**System information**

For **cobas e** 411 analyzer: test number 1680
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 261

**Intended use**

The Elecsys Zika IgG assay is an immunoassay for the in vitro qualitative detection of IgG antibodies to Zika virus in human serum and plasma. The test is intended as an aid in the diagnosis of infection with Zika virus.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

**Note**: Please note that the catalogue number appearing on the package insert retains only the first 8 digits of the licensed 11-digit Catalogue Number: 08176078190 for the Elecsys Zika IgG assay. The last 3 digits -190 have been replaced by -119 for logistic purposes.

**Summary**

Zika virus is a member of the family Flaviviridae, genus Flavivirus. The Flaviviridae family includes West Nile virus (WNV), Dengue virus (DENV), Yellow fever virus (YFV), and about 70 other viruses.[1]

Zika virus was first isolated in 1947 from a Rhesus monkey in the Zika forest of Uganda and subsequently identified in an Aedes africanus mosquito captured in that forest. The first human cases were reported during a jaundice epidemic in Eastern Nigeria in 1954.[2,3]

Zika virus is transmitted to humans by Aedes mosquito species. Aedes albopictus was described as a potential vector of Zika virus in 2007. Since 2007, other Aedes species, including Aedes aegypti, Aedes polynesiensis, Aedes dalzieli and Aedes hensilli have been reported as competent vectors of Zika virus.[4,5,6,7] The increasing presence of Aedes species, particularly of Aedes aegypti, as a vector of disease worldwide may lead to the emergence of Zika epidemics in urban areas.[8] Zika virus may be transmitted from a pregnant woman to her fetus and from a mother to a newborn at birth. Zika virus has also been detected in semen and reported to have been transmitted through sexual intercourse. In addition, Zika virus may be transmitted via transfusion and through laboratory exposure.[9,10,11]

Zika infection is asymptomatic in most (estimated 80 %) cases.[12] When symptomatic, Zika virus usually presents with non-specific, influenza-like signs and symptoms, such as mild fever, arthralgia, myalgia, headache, retro-orbital pain, conjunctivitis, abdominal pain, and a maculopapular, frequently pruritic, rash; edema and lymphadenopathy may also be present.[4] The symptoms typically appear a few days after the bite of an infected mosquito and usually last 3 to 12 days. Zika virus disease may be difficult to distinguish clinically from diseases caused by other arboviruses, including DENV, Chickungunya virus and WNV.[8] A case-control study conducted after an outbreak in French Polynesia supported a strong association of acute Zika virus infection with Guillain-Barré-Syndrome. Although symptoms in infants and children are very similar to those seen in adults, the major concerns with regard to congenital Zika virus infections are serious neurological sequelae, including, but not limited to, microcephaly, ventriculomegaly, intracranial calcifications, and ocular abnormalities.[13,14,15,16]

Serologic testing:
Laboratory evidence of Zika infection is obtained by testing samples for viral nucleic acid or virus-specific IgM and IgG antibodies. IgM levels are variable and are detectable starting near day 2 post onset of symptoms. IgG antibodies develop within days after appearance of IgM (5-8 days after the symptoms onset) and can be detected for at least months to years.[17,18] Cases have been described with persistence of IgM antibodies for a longer period which complicates differentiation of recent and prior viral infection.[19] Serology-based diagnosis of Zika virus infection poses a challenge due to the potential cross-reactivity of antibodies against related flaviviruses that are derived from natural infection or vaccination.[20]

Therefore a positive Zika IgG result may not be used as evidence for protection to a future infection by Zika virus.

**Test principle**

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 20 µL of sample, biotinylated Zika-specific recombinant antigens and Zika-specific recombinant antigens labeled with a ruthenium complex[a)] react to form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined automatically by the software by comparing the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cutoff value previously obtained by calibration.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

**Reagents - working solutions**

The reagent rackpack (M, R1, R2) is labeled as ZIKVIGG.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Zika-specific recombinant antigens (E. coli)~biotin (gray cap), 1 bottle, 9 mL:
Biotinylated Zika-specific recombinant antigens (E. coli) 0.5 mg/L; TES[b)] buffer 50 mmol/L, pH 7.2; preservative.

R2 Zika-specific recombinant antigens (E. coli)~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 9 mL:
Zika-specific recombinant antigens labeled with ruthenium complex 0.5 mg/L; TES buffer 50 mmol/L, pH 7.2; preservative.

b) TES = 2-[[1,3-dihydroxy-2-(hydroxymethyl)propane-2-yl]amino]ethanesulfonic acid

ZIKVIGG Cal1 Negative calibrator (white cap; lyophilized), 1 bottle for 1.0 mL:
Human serum, non-reactive for anti-Zika IgG antibodies; preservative.

ZIKVIGG Cal2 Positive calibrator (black cap; lyophilized), 1 bottle for 1.0 mL:
Human serum, reactive for anti-Zika IgG antibodies; preservative.

**Precautions and warnings**

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

N-Methylisothiazolone hydrochloride

EUH 208 May produce an allergic reaction.

Product safety labeling follows EU GHS guidance.

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods used assays approved by the FDA or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

The serum containing anti-Zika IgG (ZIKVIGG Cal2) was tested negative for Zika-specific RNA with NAT (nucleic acid testing).

However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[21,22]

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

**Reagent handling**

The reagents in the kit are ready-for-use (except for ZIKVIGG Cal1 and ZIKVIGG Cal2) and are supplied in bottles compatible with the system.

*Calibrators*

Carefully dissolve the contents of one bottle by adding exactly 1.0 mL of distilled or deionized water and allow to stand closed for 15 minutes to reconstitute. Mix carefully, avoiding foam formation.

Transfer the reconstituted calibrators into the supplied empty labeled snap-cap bottles.

**cobas e** 411 analyzer: The reconstituted calibrators should only be left on the analyzer during calibration at 20-25 °C. After use, close the bottles as soon as possible and store upright at 2-8 °C.

Due to possible evaporation effects, not more than 5 calibration procedures per calibrator bottle set should be performed.

If necessary, freeze in aliquots; see section on **cobas e** 601 and **cobas e** 602 analyzers.

**cobas e** 601 and **cobas e** 602 analyzers: Unless the entire volume is necessary for calibration on the analyzers, transfer aliquots of the reconstituted calibrators into empty snap-cap bottles (CalSet Vials). Attach the supplied labels to these additional bottles. Store the aliquots at -20 °C (± 5 °C) for later use.

Perform **only one** calibration procedure per aliquot.

All information required for correct operation is read in from the respective reagent barcodes.

*Please note:* Both the vial labels, and the additional labels (if available) contain 2 different barcodes. The barcode between the yellow markers is for **cobas** 8000 systems only. If using a **cobas** 8000 system, please turn the vial cap 180° into the correct position so the barcode can be read by the system. Place the vial on the instrument as usual.

**Storage and stability**

Store at 2-8 °C.

Do not freeze.

Store the Elecsys reagent kit **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

| *Stability of the reagent rackpack* | |
|---|---|
| unopened at 2-8 °C | up to the stated expiration date |
| after opening at 2-8 °C | 35 days |
| on the analyzers | 14 days |

The lyophilized calibrators are stable up to the stated expiration date.

| *Stability of the reconstituted calibrators* | |
|---|---|
| either at -20 °C (± 5 °C) | 30 days (3 freeze/thaw cycles possible) |
| or at 2-8 °C | 72 hours |
| on **cobas e** 411 at 20-25 °C | up to 5 hours |
| on **cobas e** 601 and **cobas e** 602 at 20-25 °C | use only once |

Store calibrators **upright** in order to prevent the calibrator solution from adhering to the snap-cap.

**Specimen collection and preparation**

Only the specimens listed below were tested and found acceptable.

Serum collected using standard sampling tubes or tubes containing separating gel.

Li-heparin and $K_2$-EDTA plasma as well as $K_2$-EDTA plasma tubes containing separating gel.

Criterion: Correct assignment of negative and positive samples within a recovery of ± 0.2 COI for negative and 80-120 % for positive samples.

Stable for 8 hours at 20-25 °C, 7 days at 2-8 °C, 28 days at -20 °C (± 5 °C). Freeze only once.

The sample types listed were tested with a selection of sample collection tubes or systems that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates and thawed samples before performing the assay.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

Ensure the samples, calibrators and controls are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples, calibrators and controls on the analyzers should be analyzed/measured within 2 hours.

The performance of the Elecsys Zika assay has not been established with cadaveric samples or body fluids other than serum and plasma.

**Materials provided**

See "Reagents – working solutions" section for reagents.

- 2 x 3 bottle labels
- 2 empty labeled snap-cap bottles

**Materials required (but not provided)**

- REF 08259658190, PreciControl Zika IgG, for 2 x 2.0 mL
- REF 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles
- General laboratory equipment
- **cobas e** analyzer
- Distilled or deionized water

Accessories for **cobas e** 411 analyzer:

- REF 11662988122, ProCell, 6 x 380 mL system buffer
- REF 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution
- REF 11930346122, Elecsys SysWash, 1 x 500 mL washwater additive
- REF 11933159001, Adapter for SysClean
- REF 11706802001, AssayCup, 60 x 60 reaction cups
- REF 11706799001, AssayTip, 30 x 120 pipette tips
- REF 11800507001, Clean-Liner

Accessories for **cobas e** 601 and **cobas e** 602 analyzers:

- REF 04880340190, ProCell M, 2 x 2 L system buffer
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- REF 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change
- REF 03004899190, PreClean M, 5 x 600 mL detection cleaning solution
- REF 12102137001, AssayTip/AssayCup, 48 magazines x 84 reaction cups or pipette tips, waste bags
- REF 03023150001, WasteLiner, waste bags
- REF 03027651001, SysClean Adapter M

Accessories for all analyzers:

- REF 11298500316, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

**Assay**

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use. Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers (except for the **cobas e** 602 analyzer).

**cobas e** 601 and **cobas e** 602 analyzers: PreClean M solution is necessary.

Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/ closing of the bottles.

*Calibrators:*

Place the reconstituted calibrators in the sample zone.

All the information necessary for calibrating the assay is automatically read into the analyzer.

After calibration has been performed, store the calibrators at 2-8 °C or discard (**cobas e** 601 and **cobas e** 602 analyzers).

**Calibration**

*Calibration frequency:* Calibration must be performed once per reagent lot using ZIKVIGG Cal1, ZIKVIGG Cal2 and fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer).

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Renewed calibration is recommended as follows:

- after 1 month (28 days) when using the same reagent lot
- after 7 days (when using the same reagent kit on the analyzer)
- as required: e.g. quality control findings with PreciControl Zika IgG outside the defined limits

Range for the electrochemiluminescence signals (counts) for the calibrators:
Negative calibrator (ZIKVIGG Cal1):
600-1800 (**cobas e** 411 analyzer)
400-1500 (**cobas e** 601 and **cobas e** 602 analyzers)
Positive calibrator (ZIKVIGG Cal2):
4000-40000 (**cobas e** 411 analyzer)
5000-40000 (**cobas e** 601 and **cobas e** 602 analyzers)

**Quality control**

For quality control, use PreciControl Zika IgG.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable government regulations and local guidelines for quality control.

Note: The controls are not barcode-labeled and therefore have to be run like external controls. All values and ranges have to be entered manually. Please refer to the section "QC" in the operator's manual or to the online help of the instrument software.

Non-barcode labeled controls: Only one target value and range for each control level can be entered in the analyzer. The reagent lot-specific target values have to be re-entered each time a specific reagent lot with different control target values and ranges is used. Two reagent lots with different control target values and ranges cannot be used in parallel in the same run.

The exact lot-specific target values and ranges are printed on the enclosed (or electronically available) value sheet in the reagent kit or PreciControl kit.

Please make sure that the correct values are used.

**Calculation**

The analyzer automatically calculates the cutoff based on the measurement of ZIKVIGG Cal1 and ZIKVIGG Cal2.

The result of a sample is given either as reactive or non-reactive as well as in the form of a cutoff index (COI; signal sample/cutoff).

**Interpretation of the results**

| Numeric result | Result message | Interpretation |
|---|---|---|
| COI < 1.00 | Non-reactive | Negative for anti-Zika IgG antibodies |
| COI ≥ 1.00 | Reactive | Reactive for anti-Zika IgG antibodies |

The Zika IgG results for a given specimen, as determined by assays from different manufacturers, can vary due to differences in reagents and assay methods.

**Limitations - interference**

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

*Endogenous substances*

| Compound | Concentration tested |
|---|---|
| Bilirubin | ≤ 1129 µmol/L or ≤ 66 mg/dL |
| Hemoglobin | ≤ 0.311 mmol/L or ≤ 500 mg/dL |
| Intralipid | ≤ 1500 mg/dL |
| Biotin | ≤ 900 nmol/L or ≤ 220 ng/mL |
| Rheumatoid factors | ≤ 1500 IU/mL |

Criterion: Correct assignment of negative and positive samples within a recovery of ± 0.20 COI for negative, 84-116 % for near cutoff (≥ 1.0 COI-< 10.0 COI) and 76-124 % for high positive samples (≥ 10.0 COI).

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

No false negative result due to high-dose hook effect was found with the Elecsys Zika IgG assay. Occurrence of high-dose hook effect cannot be completely excluded.

The assay was not tested for potential cross-reactivity with West Nile virus and Chikungunya virus. Infection with these organisms produce similar symptoms to those observed at the onset of Zika infection.

*Pharmaceutical substances*
In vitro tests were performed on 16 commonly used pharmaceuticals. No interference with the assay was found.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

A negative test result does not completely rule out the possibility of an infection with Zika virus. Serum or plasma samples from the very early (pre-seroconversion) phase or the late phase of a Zika virus infection can occasionally yield negative findings.

A positive Zika IgG result is not intended to be used as evidence for protection to a future infection by Zika virus.

**Specific performance data**

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

**Precision**

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84). The following results were obtained:

| **cobas e** 411 analyzer | | | | | |
|---|---|---|---|---|---|
| | | **Repeatability** | | **Intermediate precision** | |
| Sample | Mean COI | SD COI | CV % | SD COI | CV % |
| HSP[c)], negative | 0.109 | 0.008 | 7.7 | 0.011 | 10.4 |
| HSP, positive 1 | 1.01 | 0.024 | 2.4 | 0.030 | 3.0 |

# Elecsys Zika IgG

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| **cobas e** 411 analyzer | | | | | |
|---|---|---|---|---|---|
| | | **Repeatability** | | **Intermediate precision** | |
| Sample | Mean COI | SD COI | CV % | SD COI | CV % |
| HSP, positive 2 | 1.14 | 0.037 | 3.2 | 0.039 | 3.4 |
| HSP, positive 3 | 3.28 | 0.052 | 1.6 | 0.081 | 2.5 |
| HSP, positive 4 | 17.2 | 0.288 | 1.7 | 0.471 | 2.7 |
| PC[d)] Zika IgG 1 | 0.126 | 0.012 | 9.3 | 0.012 | 9.9 |
| PC Zika IgG 2 | 5.01 | 0.093 | 1.9 | 0.135 | 2.7 |

c) HSP = human specimen (serum/plasma)

d) PC = PreciControl

| **cobas e** 601 and **cobas e** 602 analyzers | | | | | |
|---|---|---|---|---|---|
| | | **Repeatability** | | **Intermediate precision** | |
| Sample | Mean COI | SD COI | CV % | SD COI | CV % |
| HSP, negative | 0.070 | 0.004 | 6.0 | 0.008 | 12.0 |
| HSP, positive 1 | 1.03 | 0.014 | 1.4 | 0.031 | 3.0 |
| HSP, positive 2 | 1.18 | 0.018 | 1.5 | 0.033 | 2.8 |
| HSP, positive 3 | 3.46 | 0.059 | 1.7 | 0.106 | 3.1 |
| HSP, positive 4 | 18.4 | 0.242 | 1.3 | 0.463 | 2.5 |
| PC Zika IgG 1 | 0.083 | 0.005 | 5.8 | 0.009 | 10.7 |
| PC Zika IgG 2 | 5.21 | 0.064 | 1.2 | 0.132 | 2.5 |

**Analytical specificity**

202 potentially cross-reacting samples characterized to be non-reactive for Zika IgG with a commercially available assay, were tested with the Elecsys Zika IgG assay. The potentially cross-reactive samples contained:

| **Disease** | **N** | **Non-reactive** | **Reactive** |
|---|---|---|---|
| Dengue virus | 30 | 30 | 0 |
| Cytomegalovirus | 12 | 12 | 0 |
| Epstein-Barr virus | 11 | 11 | 0 |
| Herpes simplex virus | 10 | 10 | 0 |
| Hepatitis A virus | 8 | 8 | 0 |
| Rubella virus | 12 | 12 | 0 |
| Hepatitis B virus | 11 | 11 | 0 |
| Hepatitis C virus | 12 | 12 | 0 |
| Malaria (Plasmodium falciparum/vivax) | 11 | 11 | 0 |
| Syphilis (Treponema pallidum) | 12 | 12 | 0 |
| Varicella zoster virus | 12 | 12 | 0 |

| **After vaccination against** | **N** | **Non-reactive** | **Reactive** |
|---|---|---|---|
| Tick-borne encephalitis virus | 20 | 20 | 0 |
| Yellow fever virus | 15 | 15 | 0 |
| Japanese encephalitis virus | 3 | 3 | 0 |

| **Autoantibodies** | **N** | **Non-reactive** | **Reactive** |
|---|---|---|---|
| Antinuclear antibodies | 12 | 12 | 0 |
| Rheumatoid factor | 11 | 11 | 0 |

An overall agreement of 100 % (202/202) was found in these specimens with the Elecsys Zika IgG assay and the comparison test.

**Agreement to comparison test**

A total of 2187 frozen samples obtained from various cohorts were tested with the Elecsys Zika IgG assay and a commercially available Zika IgG ELISA assay (6 samples with insufficient volume to complete resolution algorithm were excluded from the table and calculation).

| | | Comparison assay | | | |
|---|---|---|---|---|---|
| | | Positive | Borderline | Negative | Total |
| Elecsys Zika IgG assay | Reactive | 324 | 0 | 3 | 327 |
| | Non-reactive | 81 | 18 | 1755 | 1854 |
| | Total | 405 | 18 | 1758 | 2181 |

Overall agreement was 96.12 %. 18 borderline samples were excluded from calculation.

**Performance in samples from prevalence areas**

A total of 496 samples from patients with suspected Zika virus infection from a Zika epidemic region (LATAM) and samples from individuals from a Zika and Dengue endemic area in Africa were tested with the Elecsys Zika IgG assay and a commercially available Zika IgG ELISA assay.

99 concordant negative samples were not further tested. All 397 samples with discrepant results and concordant positive samples were further resolved with a resolution testing algorithm. 36 samples were excluded due to unresolved final result after resolution testing. 309 samples were found to be positive for anti-Zika IgG antibodies (confirmed by resolution testing). 22 samples were found to be negative discrepant with the Elecsys Zika IgG assay. These 22 samples were further tested with a commercially available line immunoblot assay; 10 samples were found to be non-reactive for Zika IgG antibodies but reactive for DENV IgG antibodies. 10 samples were identified positive for flavivirus IgG antibodies, while 2 samples remained inconclusive.

Without considering the immunoblot results, the resulting relative sensitivity and relative specificity in these cohorts was 92.88 % and 100 %, respectively.

| Cohort | N | Unresolved samples | Positive samples after resolution | Negative discrepant samples after resolution | Negative samples after resolution** |
|---|---|---|---|---|---|
| Suspected Zika infection from Zika epidemic region* | 396 | 36 | 284 | 21 | 55 |
| Zika and Dengue endemic area (Ivory Coast) | 100 | 0 | 3 | 1 | 96 |
| **Total*** | **496** | **36** | **287** | **22** | **151** |

| Cohort | N | Resolved positive / (resolved positive + negative discrepant) = relative sensitivity % | Resolved negative / (resolved negative + positive discrepant) = relative specificity % |
|---|---|---|---|
| Suspected Zika infection from Zika epidemic region* | 396 | 93.11 (89.67-95.69) | 100.00 (93.51-100.00) |
| Zika and Dengue endemic area (Ivory Coast) | 100 | 75.00 (19.41-99.37) | 100.00 (96.23-100.00) |
| **Total*** | **496** | **92.88 (89.42-95.48)** | **100.00 (97.59-100.00)** |

* 36 samples were excluded from calculation due to unresolved results after resolution testing.

** No positive discrepant samples after resolution testing.

**Relative specificity**

A total of 1685 samples (diagnostic routine and blood screening) from Europe and LATAM were tested with the Elecsys Zika IgG assay and a commercially available Zika IgG ELISA assay.

1656 concordant negative samples were detected and not further tested. All 29 samples with discrepant results and concordant positive samples were further tested with a resolution testing algorithm. 21 samples were found to be negative for anti-Zika IgG antibodies, while 2 samples were found to be

discrepant positive with the Elecsys Zika IgG assay. 6 samples were found to be positive for anti-Zika IgG antibodies and excluded from calculation.

The resulting overall relative specificity in the study was 99.88 %.

| Cohort | N | Negative samples after resolution | Positive discrepant samples after resolution | Resolved negative / (resolved negative + positive discrepant) = relative specificity % | Positive samples after resolution*** |
|---|---|---|---|---|---|
| LATAM before Zika epidemics | 94 | 92 | 0 | 100.00 (96.07-100.00) | 2 |
| European blood donors | 532 | 526 | 2 | 99.62 (98.64-99.95) | 4 |
| European blood donors with high TBE vaccination status | 559 | 559 | 0 | 100.00 (99.34-100.00) | 0 |
| European pregnant women | 500 | 500 | 0 | 100.00 (99.26-100.00) | 0 |
| Total | **1685** | **1677** | **2** | **99.88 (99.57-99.99)** | **6** |

*** 6 positive samples were excluded from relative specificity calculation.

2 remaining positive discrepant samples after resolution were classified negative for anti-Zika IgG antibodies with a commercially available line immunoblot assay.

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For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

### Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see https://usdiagnostics.roche.com for definition of symbols used):

| | |
|---|---|
| CONTENT | Contents of kit |
| SYSTEM | Analyzers/Instruments on which reagents can be used |
| REAGENT | Reagent |
| CALIBRATOR | Calibrator |
| → | Volume after reconstitution or mixing |
| GTIN | Global Trade Item Number |



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