QDx Instacheck™ Dengue IgG/IgM

INTENDED USE

QDx Instacheck™ Dengue IgG/IgM is a fluorescence Immunoassay (FIA) for the qualitative determination of IgG/IgM antibodies against dengue virus in human whole blood/serum/plasma. It is useful as an aid in screening of Dengue virus infection.
For in *vitro* diagnostic use only.

INTRODUCTION

Dengue virus (DENV), a mosquito-borne virus, phylogenetically belongs to the genus Flavivirus, including Zika virus, West Nile virus, yellow fever virus, and Japanese encephalitis virus. Dengue virus comprises of 4 serotypes distinct in the infection tendency and immune responses. Dengue virus infection causes clinically a wide range of human diseases from mild Dengue Fever (DF) to severe Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS).[1)] Several lines of evidences show that secondary Dengue virus infection, with different serotypes from the primary infection, is relevant to severe Dengue diseases.[2)] The immune response to primary or secondary virus infection varies. In the case of primary infection, specific IgM is higher titre during 4-10 days after onset of illness than IgG. IgG response become permanent for whole life of patient with primary infection. During secondary infection, in contrast, the titre of virus-specific IgG is higher than IgM titre in whole of serological period.[2,3)] Although there are many types of serological diagnostic reagents including enzyme-linked immunosorbent assay (ELISA) or immunofluorescent assays (IFA), development of simultaneous and accurate detection kit of IgG and IgM is required.[4)]

PRINCIPLE

The test uses a sandwich immunodetection method; Conjugators in conjugation pad binds to antibody in sample, forming antibody-antigen complexes, and migrates onto nitrocellulose matrix to be captured by the other immobilized-antigen on test strip.
The more antibodies in the sample, the more antigen-antibody complexes, which leads to stronger fluorescence signal. The signal then is interpreted by reader to display the 'dengue IgG/IgM positive' in the sample.

COMPONENTS AND REAGENTS

QDx Instacheck™ Dengue IgG/IgM consists of 'Cartridge', 'Diluent' and an 'ID chip'.

- The cartridge contains a test strip, the membrane which has anti-human IgM and anti-human IgG at each test lines respectively, with chicken IgY at the control line.
- Each cartridge is individually sealed in an aluminum foil pouch containing a desiccant. 25 sealed cartridges are packed in a box which also contains an ID chip.
- The diluent contains a detergent as a stabilizer and sodium azide as a preservative in sodium borate buffer.
- The diluent is dispensed into each diluent tube. 25 diluent tubes are packed in a box.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow the instructions and procedures described in this 'Instruction for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge, ID chip and diluent) should agree.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield misleading of test result(s).
- Do not reuse cartridges or diluent tubes. A diluent tube should be used for processing of one sample only. A cartridge should be used for testing one sample only
- The cartridge should remain sealed in its original pouch before use. Do not use the cartridge, if is damaged or already opened.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with the local regulations. Sample with severe hemolysis and hyperlipidemia must not be used.
- Allow the cartridge, diluent and sample to be at room temperature for approximately 30 minutes.
- The instrument for QDx Instacheck™ tests may generate slight vibration during use.
- Used cartridges, diluent tubes and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- An exposure to larger quantities of sodium azide may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure.
- **QDx Instacheck™ Dengue IgG/IgM** will provide accurate and reliable results subject to the following conditions.
  - **QDx Instacheck™ Dengue IgG/IgM** should be used only in conjunction with **QDx Instacheck™ test.**
  - Have to use recommended anticoagulant sample.

Recommended anticoagulant
EDTA, K_2 EDTA, K_3 EDTA
Sodium heparin, Lithium heparin, Sodium citrate

STORAGE AND STABILITY

Storage condition		
Component	Storage Temperature	Shelf life
Cartridge	4 - 30 °C	20 months
Diluent	4 - 30 °C	20 months

- After the cartridge pouch is opened, the test should be performed immediately.

LIMITATIONS OF THE TEST SYSTEM

- The test may yield false positive result(s) due to the cross-reactions and/or non-specific adhesion of certain sample components to the capture/detector antibodies.
- The test may yield false negative result(s) due to the non-responsiveness of the antigen to the antibodies which is most common if the epitope is masked by some unknown components, so therefore not being able to be detected or captured by the antibodies. The instability or degradation of the antigen with time and/or temperature may also cause false negative result as it makes antigen unrecognizable by the antibodies.
- Other factors may interfere with the test and cause erroneous results, such as technical/procedural errors, degradation of the test components/reagents or presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician including clinical symptoms and other relevant test results.

MATERIALS SUPPLIED

REF IFPC-34

Components of **QDx Instacheck™ Dengue IgG/IgM.**

- **Cartridge Box:**
  - Cartridges 25
  - ID Chip 1
  - Instruction for Use 1
- **Diluent tube Box:**
  - Diluent tubes 25

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **QDx Instacheck™ Dengue IgG/IgM.**
Please contact our sales division for more information.

- **QDx Instacheck™ II** REF FPRR021

SAMPLE COLLECTION AND PROCESSING

The sample type for **QDx Instacheck™ Dengue IgG/IgM** is human whole blood/serum/plasma.

- It is recommended to test the sample within 24 hours after collection
- The serum or plasma should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- The whole blood may be stored for up to a week at 2-8 °C prior to being tested.
- The serum or plasma may be stored for up to a month at 2-8 °C prior to being tested. If testing will be delayed more than a month, it should be frozen at -20 °C.
- Samples stored frozen at -20 °C for 1 year showed no performance difference.
- However, the whole blood sample should not be kept in a freezer in any case.
- Once the sample was frozen, it should be thawed one time and only for test, because repeated freezing and thawing can result in the changed test values.
- Samples containing precipitates must be clarified by centrifugation.

TEST SETUP

- Check the components of **QDx Instacheck™ Dengue IgG/IgM**: Sealed Cartridges, Diluent tubes and an ID Chip.
- Ensure that the lot number of the test cartridge matches with that of the ID chip as well as the diluent.
- Keep the sealed test cartridge (if stored in refrigerator) and the Diluent tube at room temperature for at least 30 minutes just prior to the test. Place the test cartridge on a clean, dust-free and flat surface.
- Turn on the instrument for QDx Instacheck™ tests.
  (Please refer to the 'instrument for QDx Instacheck™ tests Operation Manual' for complete information and operating instructions.)

TEST PROCEDURE

<Multi test mode>

1. Transfer 30 µL of sample (Human whole blood/serum/plasma/ control) using a pipette to the diluent tube.
2. Mix thoroughly by shaking 2~3 times.
3. Pipette out 75 µL of a sample mixture and dispense it into the sample well on the cartridge.
4. Leave the sample-loaded cartridge at room temperature for 12 minutes.
   ⚠ *Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inexact test result.*
5. To scan the sample-loaded cartridge, insert it into the cartridge holder of the instrument for QDx Instacheck™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow has been marked on the cartridge especially for this purpose.
6. Tap the 'Start' button on the instrument for QDx Instacheck™ test.
7. Instrument for QDx Instacheck™ tests will start scanning the sample-loaded cartridge immediately.
8. Read the test result on the display screen of the instrument for QDx Instacheck™ tests.

<Single test mode>

1. Transfer 30 µL of sample (whole blood/serum/plasma/control) using a pipette to the diluent tube.
2. Mix thoroughly by shaking 2~3 times.
3. Pipette out 75 µL of a sample mixture and dispense it into the sample well on the cartridge.
4. Inserting the cartridge into the holder of the instrument for QDx Instacheck™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow has been marked on the cartridge especially for this purpose.
5. Tab the 'Start' button on the instrument for QDx Instacheck™ test.
6. Instrument for QDx Instacheck™ tests will automatically start scanning the sample-loaded cartridge after 12 minutes.
7. Read the test result on the display screen of the instrument for QDx Instacheck™ tests.

※ Note: Refer to the instrument for QDx Instacheck™ tests Operation Manual to select sample type.

INTERPRETATION OF TEST RESULT

- Instrument for QDx Instacheck™ tests calculates the test result automatically and displays "G (COI value): P / N / I", "M (COI value): P / N / I".
- Ancillary value is served in the form of a cut-off index (COI).

Cut-off index (COI)	Result	Note
< 0.9	Negative for Dengue IgG / IgM	No need to additional test.
≥ 0.9, < 1.1	Indeterminate	Need to retest. If test results are shown 'Negative' or 'Indeterminate' repeatedly, these samples are considered dengue IgG/IgM antibody negative.
≥ 1.1	Positive for Dengue IgG / IgM	Need to confirmation test.

QUALITY CONTROL

- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- The control tests should be performed immediately after opening a new test lot to ensure the test performance is not altered.
- Quality control tests should also be performed whenever there is

any question concerning the validity of the test results.

- Control standards are not provided with **QDx Instacheck™ Dengue IgG / IgM**. For more information regarding obtaining the control standards, contact the technical section at Diasys Diagnostics India Private Limited.
  (Please refer to the instruction for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical sensitivity**

  - **Cut-off**
    The **QDx Instacheck™ Dengue IgG/IgM** test result indicates 'positive' or 'negative' of a sample defined by the algorithm of instrument for QDx Instacheck™ tests based on COI (cut-off index).

Cut-off index (COI)	Result
COI ≥ 1.1	Positive
0.9 ≤ COI < 1.1	Indeterminate
COI < 0.9	Negative

- **Analytical specificity**

  - **Cross-reactivity**
    There was no significant cross-reactivity from these materials with the **QDx Instacheck™ Dengue IgG/IgM** test measurements.

Cross-reactivity Materials	
#1	Anti-HAV
#2	Anti-HBV
#3	Anti-HCV
#4	Anti-EBV
#5	Anti-CMV
#6	Autonuclear antibody (ANA)
#7	Rheumatoid factor
#8	Yellow fever virus IgG
#9	Yellow fever virus IgM
#10	Chikungunya IgM

* **Chikungunya IgG**
A cross-reaction test on the chikungunya IgG showed that 10 out of 12 samples were positive. However, since 3 other reference reagents (ELISA) for the same sample have the same (positive) results, this could be a cross-reaction or coinfection.

  - **Interference**
    There was no significant cross-reactivity from these materials with the **QDx Instacheck™ Dengue IgG/IgM** test measurements.

Interference Materials	
#1	Sodium heparin
#2	K2-EDTA
#3	Sodium citrate
#4	Bilirubin
#5	Hemoglobin
#6	Triglycerides
#7	Cholesterol
#8	BSA

- **Precision**
  - Between lot
    One person tested three different lots of **QDx Instacheck™ Dengue IgG/IgM,** five times at each concentration of the control standard.
  - Between person
    Three different persons tested **QDx Instacheck™ Dengue IgG/IgM**, five times at each concentration of the control standard.
  - Between day
    One person tested **QDx Instacheck™ Dengue IgG/IgM** for three days, five times at each concentration of the control standard.
  - Between site
    One person tested **QDx Instacheck™ Dengue IgG/IgM** at three different sites, five times at each concentration of the control standard.

Standard material	**Between lot** Positive ratio	**Between person** Positive ratio	**Between day** Positive ratio	**Between site** Positive ratio
Negative	0 %	0 %	0 %	0 %
High	100 %	100 %	100 %	100 %
Mid	100 %	100 %	100 %	100 %
Low	100 %	100 %	100 %	100 %

- **Comparability**

Dengue IgG		Reference reagent (ELISA)		
		Positive	Negative	Total
QDx Instacheck™ Dengue IgG/IgM	Positive	58	0	58
	Negative	1	0	1
	Total	59	0	59
Dengue IgM		Reference reagent (ELISA)		
		Positive	Negative	Total
QDx Instacheck™ Dengue IgG/IgM	Positive	44	2	46
	Negative	8	5	13
	Total	52	7	59

- Overall agreement of IgG = 98.3 %
- Overall agreement of IgM = 83.0

REFERENCES

1. Evaluation of diagnostic test: Dengue. Rosanna W. P. et al., Nature, 2010
2. Immunoglobulin G (IgG) to IgM ratio in secondary adult dengue infection using samples from early days of symptoms onset. Cucunawangsih et al., BMC Infectious Diseases, 2015
3. Dengue Viraemia Titer, Antibody Response Pattern and Virus Serotype Correlate with Disease Severity: Vaughn. D. W. et. al., Journal of Infectious Diseases. 2000
4. Current Global Status of Dengue Diagnostics: Miranda D. S. et. al., Journal of Advance in Biology and Biotechnology, 2015

Note: Please refer to the table below to identify various symbols.

	Sufficient for <n> tests
	Read instruction for use
	Use by Date
	Batch code
	Catalog number
	Caution
	Manufacturer
	Authorized representative of the European Community
	In vitro diagnostic medical device
	Temperature limit
	Do not reuse
	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices

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