HDV IgM

“Capture” Enzyme ImmunoAssay (ELISA) for the determination of IgM antibodies to Hepatitis Delta Virus in human plasma and sera

- for “in vitro” diagnostic use only -

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HDV IgM

A. INTENDED USE
Enzyme ImmunoAssay (ELISA) for the determination of IgM class antibodies to Hepatitis Delta Virus or HDV in human plasma and sera with the "capture" system. The kit is intended for the classification of the viral infective agent and the follow-up of HDV infected patients.

For "in vitro" diagnostic use only.

B. INTRODUCTION
The Hepatitis Delta Virus or HDV is a RNA defective virus composed of a core presenting the delta-specific antigen, encapsulated by HBsAg, that requires the helper function of HBV to support its replication.

Infection by HDV occurs in the presence of acute or chronic HBV infection. When acute delta and acute HBV simultaneously occur, the illness becomes severe and clinical and biochemical features may be indistinguishable from those of HBV infection alone. In contrast, a patient with chronic HBV infection can support HDV replication indefinitely, usually with a less severe illness appearing as a clinical exacerbation.

The determination of HDV specific serological markers (HDV Ag, HDV IgM and HDV IgG) represents in these cases an important tool to the clinician for the classification of the etiological agent, for the follow up of infected patients and their treatment.

The detection of HDV IgM and IgG antibodies allows the classification of the illness and the monitoring of the seroconversion event.

C. PRINCIPLE OF THE TEST
Microplates are coated with a monoclonal anti-hIgM antibody that in the 1st incubation “captures” specifically this class of antibodies.

After washing out all the other components of the sample, in the 2nd incubation bound anti HDV IgM are detected by the addition of recombinant HDV antigen immunocomplexed with a specific antibody, labeled with peroxidase (HRP).

After washing, the enzyme captured on the solid phase, acting on the substrate/chromogen mixture, generates an optical signal that is proportional to the amount of IgM antibodies present in the sample.

D. COMPONENTS
Each kit contains sufficient reagents to carry out 96 tests.

1. Microplate: MICROPLATE
12 strips of 8 breakwells coated with purified anti human IgM specific mouse monoclonal antibody and sealed into a bag with desiccant. Allow the microplate to reach room temperature before opening; reseal unused strips in the bag with desiccant and store at 4°C.

2. Negative Control: CONTROL
1x2.0 ml/vial. Ready to use. It contains, human antibodies negative to HDV, 3% skimmed milk, 0.2M Tris buffer pH 6.0+/0.1, 0.2% Tween 20, 0.09% NaNazide and 0.1% Kathon GC as preservatives.

The Negative Control is pale yellow color coded.

3. Positive Control: CONTROL
1x2.0 ml/vial. Ready to use. It contains, human IgM antibodies positive to HDV, 3% skimmed milk, 0.2M Tris buffer pH 6.0+/0.1, 0.2% Tween 20, 0.09% NaNazide and 0.1% Kathon GC as preservatives.

The Positive Control is green yellow color coded.

Important Note: Even if this material has been chemically inactivated, handle as potentially infectious.

4. Calibrator: CAL
n° 1 vial. Lyophilized reagent to be dissolved with EIA grade water as reported in the label. It contains fetal bovine serum, human IgM antibodies to HDV, 0.2 mg/ml gentamicine sulphate and 0.1% Kathon GC as preservatives.

Important Notes:
1. The volume necessary to dissolve the content of the vial may vary from lot to lot. Please use the right volume reported on the label.
2. Even if this material has been chemically inactivated, handle as potentially infectious.

5. Wash buffer concentrate: WASHBUF 20X
1x60ml/bottle. 20x concentrated solution. Once diluted, the wash solution contains 10 mM phosphate buffer pH 7.0/-0.2, 0.05% Tween 20 and 0.1% Kathon GC.

6. Enzyme Conjugate 20X: CONJ 20X
1x0.8 ml/vial. 20X concentrated solution. Contains peroxidase labeled polyclonal antibody to HDV. The reagent is dissolved into a buffer solution 10 mM Tris buffer pH 6.8/-0.1, 5% BSA, 0.1% Kathon GC and 0.02% gentamicine sulphate as preservatives.

7. HDV Antigen: Ag HDV
1x6 vials. Lyophilized reagent to be dissolved with 1.9 ml proper diluent. It contains non infective recombinant HDV Antigen, 25 mM Tris buffer pH 7.8/-0.1 and 5% human serum proteins.

8. HDV Antigen Diluent: Ag DIL
1x16 ml/vial. Buffered solution for the dissolution of the lyophilized HDV antigen. It contains 0.2 M Tris buffer pH 6.0/-0.1, 0.1% Kathon GC and 0.2% Triton X100. The component is red colour coded.

9. Specimen Diluent: DILSPE
2x60.0 ml/vial. Buffered solution for the dilution of samples; it contains 0.2M Tris buffer pH 6.0/-0.1, 0.2% Tween 20, 3% Skimmed milk, 0.1% Kathon GC and 0.09% sodium azide as preservatives. The component is blue clour coded.

10. Chromogen/Substrate: SUBS TMB
1x16ml/vial. Contains a 50 mM citrate-phosphate buffered solution at pH 3.5-3.8, 0.03% tetra-methyl-benzidine or TMB, 4% dimethylsulphoxide and 0.02% hydrogen peroxide of H2O2.

Note: To be stored protected from light as sensitive to strong illumination.

11. Sulphuric Acid: H2SO4 0.3 M
1x15ml/vial. Contains 0.3 M H2SO4 solution.

Attention: Irritant (Xi R36/38; S2/26/30)

12. Plate sealing foils n°2

13. Package insert n°1

E. MATERIALS REQUIRED BUT NOT PROVIDED
1. Calibrated Micropipettes in the range 10-1000 ul and disposable plastic tips.
2. EIA grade water (double distilled or deionised, charcoal treated to remove oxidizing chemicals used as disinfectants).
3. Timer with 60 minute range or higher.
4. Absorbent paper tissue.
5. Calibrated ELISA microplate thermostatic incubator (dry or wet) set at +37°C.
6. Calibrated ELISA microwell reader with 450nm (reading) and if possible with 620-630nm (blanking) filters.
7. Calibrated ELISA microplate washer.
8. Vortex or similar mixing tools.
F. WARNINGS AND PRECAUTIONS

1. The kit has to be used by skilled and properly trained technical personnel only, under the supervision of a medical doctor responsible of the laboratory.

2. All the personnel involved in performing the assay have to wear protective laboratory clothes, talc-free gloves and glasses. The use of any sharp (needles) or cutting (blades) devices should be avoided. All the personnel involved should be trained in biosafety procedures, as recommended by the Center for Disease Control, Atlanta, U.S. and reported in the National Institute of Health’s publication: "Biosafety in Microbiological and Biomedical Laboratories" , ed. 1984.

3. All the personnel involved in sample handling should be vaccinated for HBV and HAV, for which vaccines are available, safe and effective.

4. The laboratory environment should be controlled so as to avoid contaminants such as dust or air-born microbial agents, when opening kit vials and microplates and when performing the test. Protect the Chromogen/Substrate (TMB/H2O2) from strong light and avoid vibration of the bench surface where the test is undertaken.

5. Upon receipt, store the kit at +2-..8° C into a temperature controlled refrigerator or cold room.

6. Do not interchange components between different lots of kits. It is recommended that components between two kits of the same lot should not be interchanged.

7. Check that the reagents are clear and do not contain visible heavy particles or aggregates. If not, advise the laboratory supervisor to initiate the necessary procedures.

8. Avoid cross-contamination between serum/plasma samples by using disposable tips and changing them after each sample.

9. Avoid cross-contamination between kit reagents by using disposable tips and changing them between the use of each one.

10. Do not excise the kit after the expiration date stated on external (primary container) and internal (vials) labels.

11. Treat all specimens as potentially infective. All human serum specimens should be handled at Biosafety Level 2, as recommended by the Center for Disease Control, Atlanta, U.S. in compliance with what reported in the Institutes of Health’s publication: "Biosafety in Microbiological and Biomedical Laboratories" , ed. 1984.

12. The use of disposable plastic labware is recommended in the preparation of the washing solution or in transferring components into other containers of automated workstations, in order to avoid contamination.

13. Waste produced during the use of the kit has to be discarded in compliance with national directives and laws concerning laboratory waste of chemical and biological substances. In particular, liquid waste generated from the washing procedure, from residuals of controls and from samples has to be treated as potentially infective material and inactivated. Suggested procedures of inactivation are treatment with a 10% final concentration of household bleach for 16-18 hrs or heat inactivation by autoclave at 121°C for 20 min...

14. Accidental spills have to be adsorbed with paper tissues soaked with household bleach and then with water. Tissues should then be discarded in proper containers designated for laboratory/hospital waste.

15. The Sulphuric Acid is an irritant. In case of spills, wash the surface with plenty of water.

16. Other waste materials generated from the use of the kit (example: tips used for samples and controls, used microplates) should be handled as potentially infective and disposed according to national directives and laws concerning laboratory wastes.

G. SPECIMEN: PREPARATION AND RECOMMENDATIONS

1. Blood is drawn aseptically by venepuncture and plasma or serum is prepared using standard techniques of preparation of samples for clinical laboratory analysis. No influence has been observed in the preparation of the sample with citrate, EDTA and heparin.

2. Avoid any addition of preservatives to samples; especially sodium azide as this chemical would affect the enzymatic activity of the conjugate.

3. Samples have to be clearly identified with codes or names in order to avoid misinterpretation of results. When the kit is used for the screening of blood units, bar code labeling and electronic reading is strongly recommended.

4. Haemolysed (red) and visibly hyperlipemic ("milky") samples have to be discarded as they could generate false results. Samples containing residues of fibrin or heavy particles or microbial filaments and bodies should be discarded as they could give rise to false results.

5. Sera and plasma can be stored at +2-..8° C for up to five days after collection. For longer storage periods, samples can be stored frozen at –20°C for several months. Any frozen samples should not be frozen/thawed more than once as this may generate particles that could affect the test result.

6. If particles are present, centrifuge at 2.000 rpm for 20 min or filter using 0.2-0.8u filters to clean up the sample for testing.

H. PREPARATION OF COMPONENTS AND WARNINGS

A study conducted on an opened kit has not pointed out any relevant loss of activity up to 6 re-uses of the device and up to 3 months.

1. **Microplate:**
   - Allow the microplate to reach room temperature (about 1 hr) before opening the container. Check that the desiccant has not turned dark green, indicating a defect in manufacturing.
   - In this case, call Dia.Pro’s customer service.
   - Unused strips have to be placed back into the aluminum pouch, with the desiccant supplied, firmly zipped and stored at +2-..8° C. When opened the first time, unused strips are stable until the humidity indicator inside the desiccant bag turns from yellow to green.

2. **Negative and Positive Controls:**
   - Ready to use. Mix well on vortex before use.

3. **Calibrator:**
   - Lyophilized reagent to be dissolved with EIA grade water as reported in the label.
   - Note: The dissolved calibrator is not stable. Store it frozen in aliquots at –20°C.

4. **Wash buffer concentrate:**
   - The whole content of the 20x concentrated solution has to be diluted with bidestilled water up to 1200 ml and mixed gently end-over-end before use.
   - During preparation avoid foaming as the presence of bubbles could impact on the efficiency of the washing cycles.
   - Note: Once diluted, the wash solution is stable for 1 week at +2-..8° C.

5. **Immunocomplex:**
   - Dissolve the lyophilized HDV Antigen with 1.9 ml HDV Antigen Diluent and mix gently in order to dissolve completely the content of the vial.
   - When all the powder is dissolved, add 100 ul 20X concentrated Enzyme Conjugate and mix gently on vortex.
Important Notes:
1. The preparation of the immunocomplex has to be carried out just after the dispensation of controls & calibrator and samples into the microplate.
2. The so prepared immunocomplex is not stable when liquid. Freeze what not used in aliquots at -20°C. Thaw only once and do not use this frozen material after the expiration date of the kit.

Specimen Diluent
Ready to use. Mix on vortex before use.

Chromogen/Substrate:
Ready to use. Mix well on vortex before use. Avoid contamination of the liquid with oxidizing chemicals, air-driven dust or microbes. Do not expose to strong light, oxidizing agents and metallic surfaces.
If this component has to be transferred use only plastic, and if possible, sterile disposable container.

Sulphuric Acid
Ready to use. Mix well on vortex before use. Attention: Irritant (X) R 36/38; S2/26/30
Legenda: R 36/38 = Irritating to eyes and skin.
S 2/26/30 = In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

I. INSTRUMENTS AND TOOLS USED IN COMBINATION WITH THE KIT
1. Micropipettes have to be calibrated to deliver the correct volume required by the assay and must be submitted to regular decontamination (70% ethanol, 10% solution of bleach, hospital grade disinfectants) of those parts that could accidentally come in contact with the sample or the components of the kit. They should also be regularly maintained in order to show a precision of 1% and a trueness of ±2%.
2. The ELISA incubator has to be set at +37°C (tolerance of ±0.5°C) and regularly checked to ensure the correct temperature is maintained. Both dry incubators and water baths are suitable for the incubations, provided that the instrument is validated for the incubation of ELISA tests.
3. The ELISA washer is extremely important to the overall performances of the assay. The washer must be carefully validated and correctly optimized using the kit controls/calibrator and reference panels, before using the kit for routine laboratory tests. Usually 4-5 washing cycles (aspiration + dispensation of 350ul/well of washing solution = 1 cycle) are sufficient to ensure that the assay performs as expected. A soaking time of 20-30 seconds between cycles is suggested. In order to set correctly their number, it is recommended to run an assay with the kit controls/calibrator and well characterized negative and positive reference samples, and check to match the values reported below in the section “Internal Quality Control”. Regular calibration of the volumes delivered and maintenance (decontamination and cleaning of needles) of the washer has to be carried out according to the instructions of the manufacturer.
4. Incubation times have a tolerance of ±5%.
5. The ELISA microplate reader has to be equipped with a reading filter of 450nm and ideally with a second filter (620-630nm) for blanking purposes. Its standard performances should be (a) bandwidth ≤ 10 nm; (b) absorbance range from 0 to ≥ 2.0; (c) linearity to ≥ 2.0; repeatability ≥ 1%. Blanking is carried out on the well identified in the section “Assay Procedure”. The optical system of the reader has to be calibrated regularly to ensure that the correct optical density is measured. It should be regularly maintained according to the manufacturer’s instructions.
6. When using an ELISA automated work station, all critical steps (dispensation, incubation, washing, reading, shaking, data handling) have to be carefully set, calibrated, controlled and regularly serviced in order to match the values reported in the section “Internal Quality Control”.

The assay protocol has to be installed in the operating system of the unit and validated as for the washer and the reader. In addition, the liquid handling part of the station (dispensation and washing) has to be validated and correctly set. Particular attention must be paid to avoid carry over by the needles used for dispensing samples and for washing. This must be studied and controlled to minimize the possibility of contamination of adjacent wells due to strongly reactive samples, leading to false positive results.
The use of ELISA automated work stations is recommended for blood screening and when the number of samples to be tested exceed 20-30 units per run.
7. Dia.Pro’s customer service offers support to the user in the setting and checking of instruments used in combination with the kit, in order to assure full compliance with the requirements described. Support is also provided for the installation of new instruments to be used with the kit.

L. PRE ASSAY CONTROLS AND OPERATIONS
1. Check the expiration date of the kit printed on the external label (primary container). Do not use if expired.
2. Check that the liquid components are not contaminated by visible particles or aggregates. Check that the Chromogen/Substrate is colorless or pale blue by aspirating a small volume of it with a sterile plastic pipette. Check that no breakage occurred in transportation and no spillage of liquid is present inside the box (primary container). Check that the aluminum pouch, containing the microplate, is not punctured or damaged.
3. Dilute all the content of the 20x concentrated Wash Solution as described above.
4. Dissolve the Calibrator as described above and gently mix.
5. Allow all the other components to reach room temperature (about 1 hr) and then mix gently on vortex all liquid reagents.
6. Set the ELISA incubator at +37°C and prepare the ELISA washer by priming with the diluted washing solution, according to the manufacturers instructions. Set the right number of washing cycles as found in the validation of the instrument for its use with the kit.
7. Check that the ELISA reader is turned on or ensure it will be turned on at least 20 minutes before reading.
8. If using an automated work station, turn on, check settings and be sure to use the right assay protocol.
9. Check that the micropipettes are set to the required volume.
10. Check that all the other equipment is available and ready to use.
11. In case of problems, do not proceed further with the test and advise the supervisor.

M. ASSAY PROCEDURE
The assay has to be performed according to the procedure given below, taking care to maintain the same incubation time for all the samples being tested.
1. Place the required number of strips in the plastic holder and carefully identify the wells for standards and samples.
2. Dilute samples 1:200 dispensing 1 ml Specimen Diluent into a disposable tube and then 5 ul sample; mix on vortex before use. Do not dilute controls/calibrator as they are ready-to-use.
3. Leave the A1 well empty for blanking purposes.
4. Pipette 100 µl of the Negative Control in triplicate. 100 µl of the Calibrator in duplicate and 100 µl of the Positive Control in single.
5. Then pipette 100 µl of diluted samples in the proper wells.
6. Finally incubate the microplate for 60 at +37°C.
Important notes:

a. Strips have to be sealed with the adhesive sealing foil, only when the test is performed manually. Do not cover strips when using ELISA automatic instruments.

b. Prepare the Immunocomplex as described.

c. When the first incubation is finished, wash the microwells as previously described (section 1.3)

8. In all the wells except A1, pipette 100 µl Immunocomplex and incubate the microplate for 60 min at +37°C.

Important note: Be careful not to touch the inner surface of the well with the pipette tip. Contamination might occur.

9. When the second incubation is over, wash the microwells as previously described (section 1.3)

10. Pipette 100 µl Chromogen/Substrate into all the wells, A1 included.

Important note: Do not expose to strong direct light as a high background might be generated.

11. Incubate the microplate protected from light at room temperature (18-24°C) for 20 min. Wells dispensed with positive samples, the Positive Control and the Calibrator as well will turn from clear to blue.

12. Pipette 100 µl Sulphuric Acid into all the wells to stop the enzymatic reaction, using the same pipetting sequence as in step 10. Addition of the stop solution will turn the Positive Control, the Calibrator and positive samples from blue to yellow.

13. Measure the colour intensity of the solution in each well, as described in section 1.5 using a 450nm filter (reading) and if possible a 620-630nm filter (background subtraction), blanking the instrument on A1.

Important notes:

1. If the second filter is not available, ensure that no finger prints are present on the bottom of the microwell before reading at 450nm. Finger prints could generate false positive results on reading.

2. Reading has should ideally be performed immediately after the addition of the Stop Solution but definitely no longer than 20 minutes afterwards. Some self oxidation of the chromogen can occur leading to a higher background.

N. ASSAY SCHEME

**Microplate**

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<tbody>
<tr>
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</table>

Legend:  
BLK = Blank  
NC = Negative Control  
CAL = Calibrator  
PC = Positive Control  
S = Sample

O. INTERNAL QUALITY CONTROL

A check is performed on the controls/calibrator any time the kit is used in order to verify whether the expected OD450nm or S/Co values have been matched in the analysis. Ensure that the following parameters are met:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blank well</td>
<td>&lt; 0.100 OD450nm</td>
</tr>
<tr>
<td>Negative Control</td>
<td>&lt; 0.200 OD450nm after blanking</td>
</tr>
<tr>
<td>Coefficient of variation</td>
<td>&lt; 30%</td>
</tr>
<tr>
<td>Calibrator</td>
<td>S/Co &gt; 2.5</td>
</tr>
<tr>
<td>Positive Control</td>
<td>&gt; 0.900 OD450nm</td>
</tr>
</tbody>
</table>

If the results of the test match the requirements stated above, proceed to the next section.

If they do not, do not proceed any further and perform the following checks:

**Problem**  
Blank well > 0.100 OD450nm  
Negative Control > 0.200 OD450nm after blanking  
Coefficient of variation > 30%

**Check**

1. that the Chromogen/Substrate solution has not become contaminated during the assay
2. that the washing procedure and the washer settings are as validated in the pre qualification study;
3. that the procedure has been correctly performed;
4. that no mistake has occurred during its distribution;  
5. that no external contamination of the standard has occurred.

**Calibrator**  
S/Co < 2.5

1. that the wash procedure and the washing settings are as validated in the pre qualification study;
2. that no mistake has occurred during its distribution;  
3. that the procedure has been correctly performed;
4. that no external contamination of the standard has occurred.

**Positive Control**  
< 0.900 OD450nm

1. that the washing procedure and the washing settings are as validated in the pre qualification study;
2. that no mistake has occurred during the distribution of the control;  
3. that no mistake has occurred during the distribution of the control;  
4. that no external contamination of the standard has occurred.

An example of dispensation scheme is reported in the table below:
If any of the above problems have occurred, report the problem to the supervisor for further actions.

P. CALCULATION OF DATA
If the test turns out to be valid, results are calculated from the mean OD450nm value of the Negative Control (NC) by means of a cut-off value (Co) determined with the following formula:

**Cut-Off = NC + 0.250**

*Important note:* When the calculation of results is performed by the operating system of an ELISA automated work station, ensure that the proper formulation is used to generate the correct interpretation of results.

Q. INTERPRETATION OF RESULTS
Test results are interpreted as a ratio of the sample OD450nm and the cut-off value (S/Co) according to the following table:

<table>
<thead>
<tr>
<th>S/Co</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.9</td>
<td>Negative</td>
</tr>
<tr>
<td>0.9 – 1.1</td>
<td>Equivocal</td>
</tr>
<tr>
<td>&gt; 1.1</td>
<td>Positive</td>
</tr>
</tbody>
</table>

A negative result indicates that the patient is not infected by HDV (acute phase).

Any patient showing an equivocal result should be retested on a second sample taken 1-2 weeks after the initial sample.

A positive result is indicative of an ongoing HDV infection and therefore the patient should be treated accordingly.

Important notes:
1. Interpretation of results should be done under the supervision of the laboratory supervisor to reduce the risk of judgement errors and misinterpretations.
2. When test results are transmitted from the laboratory to another facility, attention must be paid to avoid erroneous data transfer.
3. Diagnosis of viral hepatitis infection has to be taken and declared to the supervisor for further actions.

If any of the above problems have occurred, report the problem to the supervisor for further actions.

**Internal Gold Standard (IGS)**

<table>
<thead>
<tr>
<th>S/Co</th>
<th>Interpretation</th>
</tr>
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<tbody>
<tr>
<td>&lt; 0.9</td>
<td>Negative</td>
</tr>
<tr>
<td>0.9 – 1.1</td>
<td>Equivocal</td>
</tr>
<tr>
<td>&gt; 1.1</td>
<td>Positive</td>
</tr>
</tbody>
</table>

**2. Diagnostic Sensitivity and Specificity:**
The diagnostic performances were evaluated in a performance evaluation conducted by the Department of Gastro-Hepatology, Prof. M. Rizzetto, S. Giovanni Battista hospital, Torino, Italy, on more than 400 samples against a reference European kit.

Positive samples were collected from patients undergoing acute HDV infection.

The diagnostic specificity has been determined on panels of more than 250 negative samples from normal individuals and blood donors, classified negative with the reference kit.

Both plasma, derived with different standard techniques of preparation (citrate, EDTA and heparin), and sera have been used to determine the specificity. No false reactivity due to the method of specimen preparation has been observed.

Frozen specimens have also been tested to check whether samples freezing interferes with the performance of the test. No interference was observed on clean and particle free samples.

Samples derived from patients with different viral (HCV, HAV) and non viral pathologies of the liver that may interfere with the test were examined. No cross reaction were observed.

The Performance Evaluation study conducted in a qualified external reference center on more than 300 samples has provided the following values:

- **Sensitivity:** > 98 %
- **Specificity:** > 98 %

**3. Reproducibility:**
It has been calculated on three samples examined in replicates in different runs. The mean values obtained from a study conducted on three samples of different HDV IgM reactivity, examined in 16 replicates in three separate runs is reported below:

<table>
<thead>
<tr>
<th>Mean values</th>
<th>1st run</th>
<th>2nd run</th>
<th>3rd run</th>
<th>Average value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OD450nm</td>
<td>0.061</td>
<td>0.056</td>
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<td>Std Deviation</td>
<td>0.008</td>
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<tr>
<td>CV %</td>
<td>13.9</td>
<td>13.0</td>
<td>12.9</td>
<td>13.3</td>
</tr>
</tbody>
</table>
The variability shown in the tables did not result in sample misclassification.

S. LIMITATIONS
False positivity has been assessed as less than 2 % of the normal population, mostly due to high titers of Rheumatoid Factor. Frozen samples containing fibrin particles or aggregates may generate false positive results.

REFERENCES

This product has been manufactured by Dia. Pro s.r.l. under the controls established by a full quality management system that meets the requirements of EN-ISO 13485 as declared by the EC Notified Body n°0318

Produced by
Dia. Pro Diagnostic Bioprobes Srl.
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