

PLATELIA™ TOXO IgM 72841
96 TESTS

**QUALITATIVE DETECTION OF IgM ANTIBODIES TO
TOXOPLASMA GONDII IN HUMAN SERUM OR
PLASMA BY ENZYME IMMUNOASSAY**

IVD

BIO-RAD

1. INTENDED USE

Platelia™ Toxo IgM is an immunoassay using immunocapture format for qualitative detection of IgM antibodies to *T. gondii* in human serum or plasma.

2. CLINICAL VALUE

T. gondii is a protozoan causing infection in numerous species of mammals and birds. Toxoplasmosis, frequent in humans and animals, are more typically silent. The prevalence of this infection in the population, established using serological tests, may differ depending upon the country of origin and the age.

Toxoplasmosis during pregnancy has been implicated in serious congenital abnormalities (in particular, impaired brain functions) and sometimes stillbirth. Demonstration of Toxo IgG antibody in women prior to conception provides assurance of fetal protection from possible toxoplasmosis during pregnancy.

Predisposition to severe toxoplasmosis infection is common in persons known to have Acquired Immune Deficiency Syndrome (AIDS), or who are otherwise immunocompromised. These infections are mainly due to reactivation of *T. gondii* cysts present prior to the HIV infection.

Specific diagnosis of *T. gondii* infection can be complicated and isolation of the parasite is rare. Serologic confirmation of *T. gondii* antibody is indicative of exposure to the parasite and has become widely accepted as a means to determine immune status and susceptibility to infection. Screening of several isotypes allows either the dating of the *T. gondii* and the implementation of appropriate therapy in case of recent infection or the proposal of prophylactic recommendations: hygiene-diet guidelines in pregnant women, chemoprophylaxy in immunocompromised population.

3. PRINCIPLE

Platelia™ Toxo IgM is a qualitative test for detection of IgM antibodies to *T. gondii* in human serum or plasma by enzyme immunoassay with capture of the IgM on the solid phase.

Anti-human μ -chains antibodies are coated on the solid phase (wells of the microplate). A mixture of the *T. gondii* antigen and the monoclonal anti-*T. gondii* antigen antibody labeled with peroxylidase is used as the conjugate. The test uses the following steps :

• Step 1

Patients samples, calibrator and controls are diluted 1/21 and then distributed in the wells of the microplate. During this incubation of one hour at 37°C, IgM antibodies present in the sample bind to the anti- μ antibodies coated on the microplate wells. After incubation, IgG and other serum proteins are removed by washings.

- **Step 2**

The conjugate (mixture of *T. gondii* antigen and anti-*T. gondii* monoclonal antibody labeled with peroxidase) is added to the microplate wells. During this incubation of one hour at 37°C, the conjugate binds to the specific IgM anti-*T. gondii* antibodies that were eventually captured on the microplate. The unbound conjugate is removed by washings at the end of the incubation.

- **Step 3**

The presence of immune-complexes (Anti-human μ -chains / IgM anti-*T. gondii* / *T. gondii* Antigen / anti-*T. gondii* monoclonal antibody labeled with peroxidase) is demonstrated by the addition in each well of an enzymatic development solution.

- **Step 4**

After incubation at room temperature (+18-30°C), the enzymatic reaction is stopped by addition of 1N sulfuric acid solution. The optical density reading obtained with a spectrophotometer set at 450/620 nm is proportional to the amount of IgM antibodies to *T. gondii* present in the sample.

4. PRODUCT INFORMATION

Supplied quantities of reagents have been calculated to allow 96 tests. All reagents are exclusively for *in vitro* diagnostic use.

	Label	Nature of reagents	Presentation
R1	Microplate	Microplate: (Ready-to-use): 12 strips with 8 breakable wells, coated with anti-human μ chains	1
R2	Concentrated Washing Solution (20x)	Concentrated Washing Solution (20x): TRIS-NaCl buffer (pH 7.4), 2% Tween® 20 Preservative : < 1.5% ProClin™ 300	1 x 70 mL
R3	Negative Control	Negative Control: Human serum negative for IgM antibodies to <i>T. gondii</i> , and negative for HBs antigen, anti-HIV1, anti-HIV2 and anti-HCV Preservative : < 1.5% ProClin™ 300	1 x 0.75 mL
R4	Calibrator	Calibrator: Human serum reactive for IgM antibodies to <i>T. gondii</i> , and negative for HBs antigen, anti-HIV1, anti-HIV2 and anti-HCV Preservative : < 1.5% ProClin™ 300	1 x 0.75 mL

Label		Nature of reagents	Presentation
R5	Positive Control	Positive Control: Human serum reactive for IgM antibodies to <i>T. gondii</i> , and negative for HBs antigen, anti-HIV1, anti-HIV2 and anti-HCV Preservative : < 1.5% ProClin™ 300	1 x 0.75 mL
R6a	Antigen	T. gondii Antigen: Lyophilized <i>T. gondii</i> antigen	2 x qs 14 mL
R6b	Conjugate (101x)	Conjugate (101x): Murine monoclonal antibody anti- <i>T. gondii</i> (P30) labeled with peroxidase Preservative : < 1.5% ProClin™ 300	1 x 0.4 mL
R7	Diluent	Diluent for samples and conjugate (Ready-to-use): TRIS-NaCl buffer (pH 7.7), bovine serum albumin, 0.1% Tween® 20 and phenol red. Preservative : < 1.5% ProClin™ 300	1 x 80 mL
R9	Chromogen TMB	Chromogen (Ready-to-use): 3.3'.5.5' tetramethylbenzidine (< 0.1%), H ₂ O ₂ (<1%)	1 x 28 mL
R10	Stopping Solution	Stopping Solution (Ready-to-use): 1N sulfuric acid solution	1 x 28 mL
		Plate sealers	4

For storage conditions and expiration date, please refer to the indications stated on the box.

5. WARNINGS AND PRECAUTIONS

The reliability of the results depends on correct implementation of the following Good Laboratory Practices:

- Do not use expired reagents.
- Do not mix or associate within a given run reagents from different lots.

REMARK: For Washing Solution (R2, label identification: 20x colored green), Chromogen (R9, label identification: TMB colored turquoise) and Stopping Solution (R10, label identification: 1N colored red), it is possible to use other lots than those contained in the kit, provided these reagents are strictly equivalent and the same lot is used within a given test run.

REMARK: In addition, the Washing Solution (R2, label identification: 20x colored green) can be mixed with the 2 other washing solutions

included in various Bio-Rad reagent kits (R2, label identifications: 10x colored blue or 10x colored orange) when properly reconstituted, provided only one mixture is used within a given test run.

- Before use, wait for 30 minutes to allow reagents to reach room temperature (+18-30°C).
- Carefully reconstitute or dilute the reagents avoiding any contamination.
- Do not carry out the test in the presence of reactive vapors (acid, alkaline, aldehyde vapors) or dust that could alter the enzyme activity of the conjugate.
- Use glassware thoroughly washed and rinsed with deionized water or, preferably disposable material.
- Washing the microplate is a critical step in the procedure: follow the recommended number of washings cycles and make sure that all wells are completely filled and then completely emptied. Incorrect washings may lead to inaccurate results.
- Do not allow the microplate to dry between the end of the washings operation and the reagent distribution.
- Never use the same container to distribute the conjugate and the development solution.
- The enzymatic reaction is very sensitive to metal or metal ions. Consequently, do not allow any metal element to come into contact with the various solutions containing the conjugate or the chromogen.
- Chromogen solution (R9) should be colorless. The appearance of a blue color indicates that the reagent cannot be used and must be replaced.
- Use a new pipette tip for each sample.
- Check the pipettes and other equipments for accuracy and correct operations.

HEALTH AND SAFETY INSTRUCTIONS

Human origin material used in the preparation of reagents has been tested and found non-reactive for hepatitis B surface antigen (HBs Ag), antibodies for hepatitis C virus (anti-HCV), and to human immunodeficiency virus (anti-HIV1 and anti-HIV2). Because no method can absolutely guarantee the absence of infectious agents, handle reagents of human origin and patient samples as potentially capable of transmitting infectious diseases:

- Any material, including washings solutions, that comes directly in contact with samples and reagents containing materials of human origin should be considered capable of transmitting infectious diseases.
- Wear disposable gloves when handling samples and reagents.
- Do not pipette by mouth.
- Avoid spilling samples or solutions containing samples. Spills must be rinsed with bleach diluted to 10 %. In the event of a spill with an acid, it

must be first neutralized with sodium bicarbonate, and then cleaned with bleach diluted to 10% and dried with adsorbent paper. The material used for cleaning must be discarded in a contaminated residue container.

- Patient samples, reagents containing human origin material, as well as contaminated material and products should be discarded after decontamination only:
 - either by immersion in bleach at the final concentration of 5 % of sodium hypochloride during 30 minutes,
 - or by autoclaving at 121°C for 2 hours at the minimum.

CAUTION: Do not introduce solutions containing sodium hypochloride into the autoclave

- Avoid any contact of reagents, including those considered as not dangerous, with skin and mucosa.
- Chemical and biological residues must be handled and disposed off in accordance with Good Laboratories Practices.
- All reagents in the kit are exclusively for *in vitro* diagnostic use.



Xi - Irritant

Caution: Some of the reagents contain ProClin™ 300 < 1.5%

R43: May cause sensitisation by skin contact

S28-37: After contact with skin, wash immediately with plenty of water and soap. Wear suitable gloves

6. SAMPLES

1. Serum and plasma (EDTA, heparin or citrate) are the recommended sample types.
2. Observe the following recommendations for handling, processing and storage of blood samples:
 - Collect all blood samples observing routine precaution for venipuncture.
 - For serum, allow samples to clot completely before centrifugation.
 - Keep tubes stoppered at all times.
 - After centrifugation, separate the serum or plasma from the clot or red cells in a tightly stoppered storage tube.
 - The specimens can be stored at +2-8°C if test is performed within 7 days.
 - If test will not be completed within 7 days, or for shipment, freeze the samples at -20°C or colder.
 - Do not use samples that have been thawed more than 3 times. Previously frozen specimens should be thoroughly mixed (Vortex) after thawing prior to testing.

3. Samples containing 90 g/l of albumin or 100 mg/l of unconjugated bilirubin, lipemic samples containing the equivalent of 36 g/l of triolein (triglyceride), and hemolysed samples containing up to 10 g/l of hemoglobin do not affect the results.
4. Do not heat the samples

7. ASSAY PROCEDURE

7.1 Materials required but not provided

- Vortex mixer.
- Microplate reader equipped with 450 nm and 620 nm filters (*).
- Microplate incubator thermostatically set at $37\pm 1^{\circ}\text{C}$ (*).
- Automatic, semi-automatic or manual microplate washer (*).
- Sterile distilled or deionized water.
- Disposable gloves.
- Goggles or safety glasses.
- Adsorbent paper.
- Automatic or semi-automatic, adjustable or preset, pipettes or multi-pipettes, to measure and dispense 10 μL to 1000 μL , and 1 mL, 2 mL and 10 mL.
- Graduated cylinders of 25 mL, 50 mL, 100 mL and 1000 mL capacity.
- Sodium hypochloride (bleach) and sodium bicarbonate.
- Container for biohazard waste.
- Disposable tubes.

(*) Consult our technical department for detailed information about the recommended equipment.

7.2 Reagents reconstitution

- **R1:** Allow 30 minutes at room temperature ($+18-30^{\circ}\text{C}$) before opening the bag. Take out the carrier tray, return unused strips in the bag immediately and check the presence of desiccant. Carefully reseal the bag and store it at $+2-8^{\circ}\text{C}$.
- **R2:** Dilute 1/20 the washing solution R2 in distilled water: for example 50 mL of R2 and 950 mL of distilled water to get the ready-to-use washing solution. Prepare 350 mL of diluted washing solution for one plate of 12 strips if washing manually.
- **R3, R4, R5:** Dilute 1/21 in Diluent (R7) (example: 300 μL of R7 + 15 μL of Calibrator or Control).
- **R6a:** *T. gondii* Antigen is lyophilized. For running 6 strips, reconstitute one vial of lyophilized antigen by adding 14 mL of Diluent (R7). Mix thoroughly. Once diluted, the antigenic solution (R6a+R7) must be perfectly clear.

- **R6 (R6a+R6b)** - Conjugate working solution: Add 140 μL of conjugate (R6b) to each vial of reconstituted *T. gondii* antigen (diluted R6a). Mix thoroughly. The conjugate working solution must be reconstituted at least 1 hour before use.

7.3 Storage and validity of opened and / or reconstituted reagents

The kit must be stored at $+2-8^{\circ}\text{C}$. When the kit is stored at $+2-8^{\circ}\text{C}$ before opening, each component can be used until the expiration date indicated on the outer label of the kit.

- **R1:** Once opened, the strips remain stable for up to 8 weeks if stored at $+2-8^{\circ}\text{C}$ in the same carefully closed bag (check the presence of desiccant).
- **R2:** Once diluted, the Washing Solution can be kept for 2 weeks at $+2-30^{\circ}\text{C}$. Once opened, the concentrated Washing Solution stored at $+2-30^{\circ}\text{C}$, in absence of contamination, is stable until the expiration date indicated on the label.
- **R3, R4, R5, R6b, R7:** Once opened and without any contamination, the reagents stored at $+2-8^{\circ}\text{C}$ are stable for up to 8 weeks.
- **R6 (R6a+R6b):** Once reconstituted, the conjugate working solution is stable for 8 hours at room temperature ($+18-30^{\circ}\text{C}$) or 4 weeks at $+2-8^{\circ}\text{C}$.
- **R9:** Once opened and without any contamination, the reagent stored at $+2-8^{\circ}\text{C}$ is stable for up to 8 weeks.
- **R10:** Once opened and without any contamination, the reagent stored at $+2-8^{\circ}\text{C}$ is stable until the expiration date indicated on the label.

7.4 Procedure

Strictly follow the assay procedure and Good Laboratory Practices.

Before use, allow reagents to reach room temperature ($+18-30^{\circ}\text{C}$).

The use of breakable wells requires a special attention during handling.

Use calibrator and controls with each run to validate the assay results.

1. Carefully establish the distribution and identification plan for calibrator, controls and patients samples.
2. Prepare the diluted Washing Solution (R2) [Refer to Section 7.2].
3. Take the carrier tray and the strips (R1) out of the protective pouch [Refer to Section 7.2].
4. Prepare the conjugate working solution R6 (R6a+R6b) [Refer to Section 7.2].
5. In individually identified tubes, dilute Calibrator (R4) and Controls (R3, R5) and patients samples (S1, S2...) in Diluent (R7) to give a 1/21 dilution: 300 μL of Diluent (R7) and 15 μL of sample. Vortex diluted samples.
6. Strictly following the indicated sequence below, distribute in each well with 200 μL of diluted calibrator, controls and patient samples:

	1	2	3	4	5	6	7	8	9	10	11	12
A	R3	S5	S13									
B	R4	S6										
C	R4	S7										
D	R5	S8										
E	S1	S9										
F	S2	S10										
G	S3	S11										
H	S4	S12										

- Cover the microplate with an adhesive plate sealer, then press firmly onto the plate to ensure a tight seal. Incubate the microplate immediately in a thermostat controlled water bath or in a dry incubator for 1 hour \pm 5 minutes at $37^{\circ}\text{C} \pm 1^{\circ}\text{C}$.
- At the end of the first incubation period, remove the adhesive plate sealer. Aspirate the content of all wells into a container for biohazard waste (containing sodium hypochloride). Wash microplate 4 times with 350 μL of the Washing Solution (R2). Invert the microplate and gently tap on adsorbent paper to remove remaining liquid.
- Distribute immediately 200 μL of the conjugate working solution (R6) in all wells. The solution must be shaken gently before use.
- Cover the microplate with an adhesive plate sealer, then press firmly onto the plate to ensure a tight seal. Incubate the microplate immediately in a thermostat controlled water bath or in a dry incubator for 1 hour \pm 5 minutes at $37^{\circ}\text{C} \pm 1^{\circ}\text{C}$.
- At the end of the second incubation period, remove the adhesive plate sealer. Aspirate the content of all wells into a container for biohazard waste (containing sodium hypochloride). Wash microplate 4 times with 350 μL of the Washing Solution (R2). Invert the microplate and gently tap on adsorbent paper to remove remaining liquid.
- Quickly distribute into each well and **away from light** 200 μL of Chromogen solution (R9). **Allow the reaction to develop in the dark for 30 ± 5 minutes at room temperature ($+18-30^{\circ}\text{C}$).** Do not use adhesive plate sealer during this incubation.
- Stop the enzymatic reaction by adding 100 μL of Stopping Solution (R10) in each well. Use the same sequence and rate of distribution as for the development solution.
- Carefully wipe the plate bottom. Read the optical density at 450/620 nm using a plate reader within 30 minutes after stopping the reaction. The strips must always be kept away from light before reading.

15. Before reporting results, check for agreement between the reading and the distribution plan of plate and samples.

8. INTERPRETATION OF RESULTS

8.1 Calculation of the Cut-Off value (CO)

The Cut-Off value (CO) corresponds to the mean value of the optical densities (OD) of the cut-off Control duplicates (R4):

$$\text{CO} = \text{mean of OD R4}$$

8.2 Calculation of the Sample Ratio

Sample result is expressed by Ratio using the following formula:

$$\text{Sample Ratio} = \text{Sample OD/CO}$$

8.3 Quality Control

Include the calibrator and controls for each microplate and for each run, and analyse the obtained results. For validation of the assay, the following criteria must be met:

- Optical density values:

$$\text{CO} \geq 0.300$$

$$0.80 \times \text{CO} < \text{OD R4 Repl.1} < 1.20 \times \text{CO}$$

$$0.80 \times \text{CO} < \text{OD R4 Repl.2} < 1.20 \times \text{CO}$$

(Individual OD of each replicate of the Cut-Off control (R4) must not differ more than 20% of the CO value).

- Optical density ratios:

$$\text{Ratio R3 (OD R3 / CO)} \leq 0.30$$

$$\text{Ratio R5 (OD R5 / CO)} \geq 1.80$$

If those quality control criteria are not met, the test run should be repeated.

8.4 Interpretation of results

Sample Ratio	Result	Interpretation
Ratio < 0.80	Negative	The sample is considered non reactive for the presence of IgM antibodies to <i>T. gondii</i> .
$0.80 \leq \text{Ratio} < 1.00$	Equivocal	The sample is considered equivocal for the presence of IgM antibodies to <i>T. gondii</i> . The result must be confirmed by another test done on a second sample drawn at least 3 weeks later after the first examination.
Ratio ≥ 1.00	Positive	The sample is considered reactive for the presence of IgM antibodies to <i>T. gondii</i> .

8.5 Trouble Shooting Guide

Non validated or non repeatable reactions are often caused by:

- Inadequate microplate washings.
- Contamination of negative samples by serum or plasma with a high antibody titer.
- Contamination of the development solution by chemical oxidizing agents (bleach, metal ions...).
- Contamination of the Stopping Solution.

9. PERFORMANCES

Performances of Platelia™ Toxo IgM were evaluated at 2 sites using a total of 863 samples from pregnant women and blood donors. Additionally, performance of Platelia™ Toxo IgM was evaluated on 47 cord blood samples.

9.1 Prevalence

Prevalence of anti-Toxo IgM antibodies using Platelia™ Toxo IgM was estimated on a panel of 500 samples from pregnant women. 15 samples were positive for anti-Toxo IgM antibodies. Prevalence measured with Platelia™ Toxo IgM assay is established at 3% (15/500).

9.2 Specificity

Specificity was estimated using a panel of 737 samples found negative with Platelia™ Toxo IgM TMB (72751) from 2 sites located in France and split as follows:

- 154 sera from blood donors
- 583 sera from pregnant women

Tested population / site		Number of sera	Negative	Equivocal	Positive	Specificity
Site 1	Pregnant women	102	102	0	0	100.0% (102/102) [97.1%-100%]
	Blood donors	154	154	0	0	100.0% (154/154) [98.1%-100%]
Site 2	Pregnant women	481	480	1	0	99.8% (480/481) [99.8%-99.9%]
Total		737	736	1	0	99.9% (736/737) [99.25%-100%]

* Equivocal results were considered as positive for calculation of specificity.

[IC 95%] = 95% confidence interval.

9.3 Sensitivity

Sensitivity was estimated using a panel of 69 samples found positive with Platelia™ Toxo IgM TMB (72751), from 2 sites located in France and split as follows:

- 4 sera from blood donors
- 65 sera from pregnant women

		Platelia™ Toxo IgM TMB (72751)		
		Equivocal*	Positive	Total
Platelia™ Toxo IgM (72841)	Negative	0	0	0
	Equivocal*	8	0	8
	Positive	1	60	61
	Total	9	60	69

Relative sensitivity: 69/69 100,0% [IC 95% = 94,8% - 100,0%]

* *Equivocal results were considered as positive for calculation of sensitivity.*
[IC95%] = 95% confidence interval.

The discrepant positive sample with Platelia™ Toxo IgM assay was confirmed positive with an ISAGA method.

In addition, 57 samples from a panel of 19 seroconversions were tested. Among these 19 seroconversions, 18 were detected in a comparable way and one seroconversion presented a shift of one sample in favour of the reference method.

9.4 Performances on cord blood samples

47 cord blood samples were tested using the protocol described in Section 7.4 (sample dilution 1:21):

- 22 samples from confirmed congenital toxoplasmosis
- 18 samples from maternal toxoplasmosis past-infection
- 7 samples with no infection

20 samples from congenital toxoplasmosis were either positive (18) or equivocal (2) using Platelia™ Toxo IgM assay (72841). However, all the samples from past-infections or non-infection were found negative.

	Platelia™ Toxo IgM (72841)			Platelia™ Toxo IgG (72840)		
	Positive	Doubtful	Negative	Positive	Doubtful	Negative
Congenital toxoplasmosis (n=22)	18	2	2	22	0	0
Maternal past-infection (n=18)	0	0	18	18	0	0
Negative (n=7)	0	0	7	0	0	7

9.5 Cross Reactivity

A panel of 205 samples including 167 positive samples for CMV, Rubella, EBV, HSV, VZV, mumps, measles and HIV and 38 positive samples for rheumatoid factor, auto-antibodies and heterophile antibodies along with myeloma samples were tested with Platelia™ Toxo IgM and a commercialized EIA assay for screening of anti-*T. gondii* IgM antibodies.

Among these samples, 2 were found positive and concordant with the EIA kit used for comparison: 1 sample positive for anti-EBV and 1 sample positive for anti-HSV 2 IgG.

9.6 Precision

- Within-run precision (repeatability):

In order to evaluate intra-assay repeatability, one negative and three positive samples were tested 32 times during the same run. The ratio (Sample OD/CO) was determined for each sample. Mean of ratio, Standard Deviation (SD) and Coefficient of Variation (%CV) for each specimen are listed in the table below:

Within-run precision (repeatability)

N=32	Negative Sample	Low Positive sample	Positive sample	High Positive Sample
	Ratio (Sample OD/CO)			
Mean	0.05	1.92	3.23	4.49
SD	0	0.04	0.07	0.10
% CV	5.0%	2.1%	2.3%	2.3%

- Between-run precision (reproducibility) :

In order to evaluate inter-assay reproducibility, the four samples (one negative and three positive) were tested in duplicate in two runs per day over a 20 days period. The concentration (IU/ml) was determined for each sample. Mean of concentrations (IU/ml), Standard Deviation (SD) and Coefficient of Variation (%CV) for each specimen are listed in the table below:

Between-run precision (reproducibility)

N=80	Negative Sample	Low Positive sample	Positive sample	High Positive Sample
	Ratio (Sample OD/CO)			
Mean	0.04	2.05	3.28	4.64
SD	0.01	0.06	0.10	0.14
% CV	21.0%	2.8%	3.1%	3.0%

10. LIMITATIONS OF THE PROCEDURE

Diagnosis of *T. gondii* infection can only be established on the basis of a combination of clinical and biological data. The result of a single test of titration of anti-*T. gondii* IgM antibodies does not constitute sufficient proof for the diagnosis of a recent infection.

- Diagnosis of a recent infection can only be made with complete patient information including clinical and biological data (significant increase of anti-*T. gondii* IgG antibodies on 2 patient sera drawn at 3 weeks interval and tested in the same run, presence of anti-*T. gondii* IgM at a significant level, demonstration of low IgG avidity).
- Presence of anti-*T. gondii* IgM antibodies does not constitute a sufficient proof to confirm a recent infection because IgM can persist several months or even years after infection. When IgM are detected, a quantitative determination of anti-*T. gondii* IgG antibodies should be performed, as well as a follow-up of the evolution of anti-*T. gondii* antibodies on at least a second serum sampled three weeks later.
- If a sample is tested too early during a recent primo-infection, anti-*T. gondii* IgM antibodies could be not yet present. If a suspicion exists, a second sample should be drawn about 3 weeks later on which IgM testing will be performed again.

11. QUALITY CONTROL OF THE MANUFACTURER

All manufactured reagents are prepared according to our Quality System, starting from reception of raw material to commercialization of the final product. Each lot is submitted to quality control assessments and is released to the market only after conforming to pre-defined acceptance criteria.

The records related to production and controls of each single lot are kept within Bio-Rad.

12. REFERENCES

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CE

- (US) - CE marking (European directive 98/79/CE on *in vitro* diagnostic medical devices)
- (F) - Marquage CE (Directive européenne 98/79/CE relative aux dispositifs médicaux de diagnostic *in vitro*)
- (E) - Marcado CE (Directiva europea 98/79/CE sobre productos sanitarios para diagnóstico *in vitro*)
- (I) - Marchiatura CE (Direttiva europea 98/79/CE relativa ai dispositivi medico-diagnostici *in vitro*)
- (D) - CE Konformitätskennzeichnung (Europäische Richtlinie 98/79/EG über *In-vitro*-Diagnostika)
- (P) - Marcação CE (Directiva europea 98/79/CE relativa aos dispositivos médicos de diagnóstico *in vitro*)
- (S) - CE-märkning (Europeiskt direktiv 98/79/EG om medicintekniska produkter för *in vitro*-diagnostik)
- (DK) - CE-mærkingen (Europa direktiv 98/79/EF om medicinsk udstyr til *in vitro*-diagnostik)
- (GR) - Χαρακτηρισμός CE (ευρωπαϊκή οδηγία 98/79/CE περί *in vitro* διαγνωστικών ιατρικών συσκευών)
- (PL) - CE oznaczenie (Dyrektywa unijna 98/79/CE dotycząca produktów medycznych do badań *in vitro*)
- (LT) - CE ženklas (Europos sąjungos direktyva 98/79/CE dėl *in vitro* diagnostikos medicinos prietaisų)
- (H) - CE jelzés (98/79/CE Európai Irányelv az *in vitro* orvosi diagnosztikai eszközökről)
- (EST) - CE märgistus (Euroopa direktiiv 98/79/CE *in vitro* diagnostikameditsiiniseadmete kohta)
- (SK) - CE označenie o zhode (Európska direktíva 98/79/CE pre *in vitro* diagnostické zdravotnícke postupy)
- (CZ) - CE značka (Evropská direktiva 98/79/CE o diagnostických zdravotnických prostředcích *in vitro*)
- (N) - CE-merking (EU-direktiv 98/79/CE om medisinsk utstyr til *in vitro*-diagnostikk)
- (RO) - Marca CE (Directiva europeana 98/79/CE pentru dispozitive medicale de diagnostic *in vitro*)
- (BG) - CE маркировка (Европейска директива 98/79/CE за *in vitro* диагностичните медицински изделия)

IVD

- (US) - For *in vitro* diagnostic use
- (F) - Pour diagnostic *in vitro*
- (E) - Para diagnóstico *in vitro*
- (I) - Per uso diagnostico *in vitro*
- (D) - In-vitro-Diagnostikum
- (P) - Para uso em diagnóstico *in vitro*
- (S) - *In vitro*-diagnostik
- (DK) - *In vitro* diagnose
- (GR) - Για *in vitro* διαγνωστική χρήση
- (PL) - Do stosowania *in vitro*
- (LT) - *in vitro* diagnostikai
- (H) - Csak *in vitro* diagnosztikai alkalmazásra
- (EST) - *In vitro* diagnostiliseks kasutamiseks
- (SK) - Na diagnostiku *in vitro*
- (CZ) - Pro diagnostiku *in vitro*
- (N) - Til *in vitro*-diagnostikk
- (RO) - Pentru diagnostic *in vitro*
- (BG) - За *in vitro* диагностика

REF

- (US) - Catalogue number
- (F) - Référence catalogue
- (E) - Número de catálogo
- (I) - Numero di catalogo
- (D) - Bestellnummer
- (P) - Número de catálogo
- (S) - Katalognummer
- (DK) - Katalognummer
- (GR) - Αριθμός καταλόγου
- (PL) - Numer katalogu
- (LT) - Katalogo numeris
- (H) - Cikkszám
- (EST) - Katalooginumber
- (SK) - Katalógové číslo
- (CZ) - Katalógové číslo
- (N) - Katalognummer
- (RO) - Număr de catalog
- (BG) - Каталоген номер



EC REP

- (US) - Manufacturer
- (F) - Fabricant
- (E) - Fabricante
- (I) - Produttore
- (D) - Hersteller
- (P) - Fabricante
- (S) - Tillverkad av
- (DK) - Fremstillet af
- (GR) - Κατασκευαστής
- (PL) - Producent
- (LT) - Gamintojas
- (H) - Gyártó
- (EST) - Tootja
- (SK) - Výrobca
- (CZ) - Výrobce
- (N) - Produsent
- (RO) - Producător
- (BG) - Производител

- (US) - Authorised Representative
- (F) - Représentant agréé
- (E) - Representante autorizado
- (I) - Distributore autorizzato
- (D) - Bevollmächtigter
- (P) - Representante Autorizado
- (S) - Auktoriserad representant
- (DK) - Autoriseret repræsentant
- (GR) - Εξουσιοδοτημένος αντιπροσωπός
- (PL) - Uprawniony Przedstawiciel
- (LT) - Įgaliotasis atstovas
- (H) - Meghatalmazott Képviselő
- (EST) - Volitatud esindaja
- (SK) - Autorizovaný zástupca
- (CZ) - Zplnomocněný zástupce
- (N) - Autorisert representant
- (RO) - Reprezentant autorizat
- (BG) - Упълномощен представител

LOT



- (US) - Batch code
- (F) - Code du lot
- (E) - Código de lote
- (I) - Codice del lotto
- (D) - Chargen-Bezeichnung
- (P) - Código do lote
- (S) - Batchnr
- (DK) - Batchkoden
- (GR) - Κωδικός παρτίδας
- (PL) - Numer serii
- (LT) - Serijos numeris
- (H) - Gyártási szám
- (EST) - Partii kood
- (SK) - Číslo šarže
- (CZ) - Číslo šarže
- (N) - Partikode
- (RO) - Număr de lot
- (BG) - Партиден номер

- (US) - Expiry date YYYY/MM/DD
- (F) - Date de peremption AAAA/MM/JJ
- (E) - Estable hasta AAAA/MM/DD
- (I) - Da utilizzare prima del AAAA/MM/GG
- (D) - Verwendbar bis JJJJ/MM/TT
- (P) - Data de expiração AAAA/MM/DD
- (S) - Utgångsdatum ÅÅÅÅ/MM/DD
- (DK) - Anvendes før ÅÅÅÅ/MM/DD
- (GR) - Ημερομηνία λήξης YYYY/MM/DD
- (PL) - Data ważności YYYY/MM/DD
- (LT) - Galioja iki YYYY/MM/DD
- (H) - Szavatossági idő ÉÉÉÉ/HH/NN
- (EST) - Aegumistähtaeg AAAA/KK/PP
- (SK) - Použitelné do RRRR/MM/DD
- (CZ) - Datum expirace RRRR/MM/DD
- (N) - Utløpsdato ÅÅÅÅ/MM/DD
- (RO) - Data expirării AAAA/LL/ZZ
- (BG) - Срок на годност година/месец/ден



- (US) - Storage temperature limitation
(F) - Limites de températures de stockage
(E) - Temperatura limite
(I) - Limiti di temperatura di conservazione
(D) - Lagertemperatur
(P) - Limites de temperatura de armazenamento
(S) - Temperaturbegränsning
(DK) - Temperaturbegrænsning
(GR) - Περιορισμός θερμοκρασίας αποθήκευσης
(PL) - Temperatura przechowywania
(LT) - Saugojimo temperatūriniai apribojimai
(H) - Tárolási hőmérsékleti határok
(EST) - Päärdavustemperatuurilise
(SK) - Skladovacia teplota od do
(CZ) - Teplotní rozmezi od do
(N) - Oppbevaringstemperatur
(RO) - Limitele de temperatură la stocare
(BG) - Температурни граници на съхранение



- (US) - Consult Instruction for use
(F) - Consulter le mode d'emploi
(E) - Consulte las instrucciones de uso
(I) - Consultare le istruzioni per uso
(D) - Siehe Gebrauchsanweisung
(P) - Consulte o folheto informativo
(S) - Se bruksanvisningen
(DK) - Se instruktion for brug
(GR) - Συμβουλευθείτε τις οδηγίες χρήσης
(PL) - Sprawdź instrukcję
(LT) - Iškokite informacijos vartojimo instrukcijoje
(H) - Olvassa el a használati utasítást
(EST) - Kasutamisel vaata instruksiooni
(SK) - Katalógové číslo
(CZ) - Viz návod k použití
(N) - Se bruksanvisninger
(RO) - Consultati prospectul de utilizare
(BG) - Виж инструкцията за употреба

- (US) - The other languages which are required in conformity to the European Directive can be obtained from your local Bio-Rad agent.
- (F) - Les autres langues requises par la Directive Européenne sont disponibles auprès de votre représentant Bio-Rad local.
- (E) - Los otros idiomas que se requieren para la conformidad de la Directiva Europea puede ser obtenida en su oficina local Bio-Rad.
- (I) - Le altre lingue che sono richieste in conformità con le Direttive Europee possono essere ottenute dal locale agente Bio-Rad.
- (D) - Die anderen Sprachen, die in Übereinstimmung mit der europäischen IVD Direktive benötigt werden, erhalten Sie über Ihre lokale Bio-Rad Niederlassung.
- (P) - As restantes línguas, obrigatórias em conformidade com a Directiva Europeia, podem ser obtidas através da subsidiária Bio-Rad mais próxima de si.
- (S) - Övriga språk som krävs i enlighet med EG-direktivet kan erhållas från din lokala Bio-Rad-representant.
- (DK) - De øvrige sprog som kræves i henhold til EU direktiv kan fås ved henvendelse til den lokale Bio-Rad leverandør.
- (GR) - Τις υπολοίπες γλώσσες που απαιτούνται για συμμορφωση στην ευρωπαϊκή οδηγία μπορείτε να τις προμηθευθείτε από τον τοπικό σας αντιπρόσωπο Bio-Rad.
- (PL) - Tłumaczenie w innych językach które są wymagane w Dyrektywie Unijnej może być otrzymane od lokalnego przedstawiciela firmy Bio-Rad.
- (LT) - Vertimus, reikalingus pagal Europos sąjungos direktyvos reikalavimus, į kitas kalbas galite gauti iš vietinio Bio-Rad atstovo.
- (H) - A leírás az Európai Irányelv által előírt egyéb nyelveken hozzáférhető a Bio-Rad helyi kirendeltségénél.
- (EST) - Teised vastavaalt Euroopa Direktiivile nõutavad keeled on saadaval kohaliku Bio-Radi edasimüüja käest.
- (SK) - Ostatné jazykové verzie, ktoré sú vyžadované v zhode s Európskou direktívou, možno obdržať od vášho lokálneho zástupcu Bio-Rad.
- (CZ) - Další jazykové verze vyžadované ve shodě s evropskou direktivou jsou k dispozici u lokálního zástupce firmy Bio-Rad.
- (N) - Övriga språk som kreves i henhold til EU-direktivet, fås fra din lokale Bio-Rad-representant.
- (RO) - Alte traduceri cerute în conformitate cu Directiva Europeană se pot obține de la Reprezentanța Bio-Rad locală.
- (BG) - Останалите езици, които се изискват съгласно Европейската Директива, могат да Ви бъдат предоставени от локалния представител на Био-Рад.

Bio-Rad

3, boulevard Raymond Poincaré
92430 Marnes-la-Coquette France

Tel. : +33 (0) 1 47 95 60 00

Fax.: +33 (0) 1 47 41 91 33



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