Instructions for Use

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HMGB1 express ELISA

Enzyme immunoassay for the quantitative determination of HMGB1 in human serum and plasma (EDTA, Citrate).

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Σ **96**

2°C 8°C

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REVISION HISTORY OF INSTRUCTIONS FOR USE

Changes from the previous version 2021-01 to actual version 2023-07
Chapter 5 Additional information Chapter 14 Additional information

1. INTENDED USE

Enzyme immunoassay for the quantitative determination of HMGB1 in human serum and plasma (EDTA, Citrate).

2. SUMMARY AND EXPLANATION

In 1973 a group of non-histone nuclear protein with high electrophoretic mobility was discovered and termed High-Mobility Group (HMG9 proteins [1]. The High Mobility Group Box1 Protein (HMGB1) ubiquitous small protein (30 kDa) that is the major component of the non-histone nuclear protein group. The protein is ubiquitously expressed in eukaryotes and hereby serves a plethora of different functions within the subcellular localizations [2]. HMGB1 can easily shuttle between the nucleus and cytoplasm [3] and is widely expressed in various tissues [4].

Within the nucleus HMGB1 is involved in the DNA-binding and folding activity, as well as a regulator of various key DNA processes (recombination, repair, transcription, gene expression and genomic stability) [1]. However, once released into the cytoplasm by immunocompetent cells HMGB1 is involved in disease pathogenesis and inflammation (damage-associated molecular pattern (DAMP) [2]. It also serves as a necrosis marker [5] and is involved in immune response processes (liver failure, rheumatoid arthritis, acute lung injury) and disseminated intravascular coagulation [6] and measured in case of an drug-induced liver failure [7].

Significant clinical value has HMGB1 in case of an Drug-induced liver injury (DILI). DILI, the first cause of acute liver failure, refers to liver injury caused by drugs or chemical agents e.g. Acetaminophen overdose [6 ; 8].

According to the IMI SAFE-T consortium in collaboration with DILIN and PSTC evaluated new liver safety biomarkers, which includes HMGB1 (beside osteopontin, keratin 18 and MCSFR1, miR-122 and GLDH) as i) a marker of progression prediction from hepatocellular injury to severe DILI and ii.) prediction of the occurrence of suspected intrinsic liver injury (EASL Clinical Practice Guidelines) [9].

3. TEST PRINCIPLE

HMGB1 express ELISA is a sandwich-enzyme immunoassay for the quantitative determination of HMGB1 in serum and plasma. The wells of the microtiter strips are coated with purified anti-HMGB1 antibody. HMGB1 in the sample binds specifically to the immobilized antibody and is recognized by a second enzyme marked antibody. After substrate reaction the HMGB1 concentration is determined by the colour intensity.

4. WARNINGS AND PRECAUTIONS

1. For *in-vitro diagnostic* use only. For professional use only.
2. Before starting the assay, read the instructions completely and carefully. Use the valid version of the package insert provided with the kit. Be sure that everything is understood.
3. In case of severe damage of the kit package please contact IBL or your supplier in written form, latest one week after receiving the kit. Do not use damaged components in test runs, but keep safe for complaint related issues.
4. Broken glass may cause injury. Handle glass vessels with caution.
5. Obey lot number and expiry date. Do not mix reagents of different lots. Do not use expired reagents.
6. Follow good laboratory practice and safety guidelines. Wear lab coats, disposable latex gloves and protective glasses where necessary.
7. Reagents of this kit containing hazardous material may cause eye and skin irritations. See MATERIALS SUPPLIED and labels for details. Safety Data Sheets for this product are available on the IBL-Homepage or upon request directly from IBL.
8. Chemicals and prepared, used, unused or expired reagents have to be treated as hazardous waste according to national biohazard and safety guidelines or regulations.
9. The cleaning staff should be guided by the professionals regarding potential hazards and handling.
10. All serious incidents that have occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.
11. Avoid contact with Stop solution. It may cause skin irritations and burns.
12. All reagents of this kit containing human serum or plasma have been tested and were found negative for anti-HIV I/II, HBsAg and anti-HCV. However, a presence of these or other infectious agents cannot be excluded absolutely. For this reason reagents should be treated as potential biohazards in use and for disposal.
13. Some reagents contain ProClin 300 as preservative. In case of contact with eyes or skin, flush immediately with water. When disposing reagents, flush with a large volume of water to avoid built-up.
14. The device contains material of animal origin, which is certified apparently free of infectious or contagious diseases and injurious parasites. Still the material should be handled with extreme caution.

5. STORAGE AND STABILITY

The kit is shipped at ambient temperature and should be stored at 2 - 8°C. Keep away from heat or direct sunlight. The storage and stability of specimens and prepared reagents is stated in the corresponding chapters.

The unopened reagents are stable until the expiry date indicated. The kit is stable up to 6 months after the first opening (not exceeding the expiry date) when the Microtiterplate is packed in a tightly closed bag, the bottles are closed with their screw caps and the kit is stored at indicated storage temperature.

6. SPECIMEN COLLECTION AND STORAGE

Serum, Plasma (EDTA, Citrate)

Specimen collection

The usual precautions for venipuncture should be observed. It is important to preserve the chemical integrity of a blood specimen from the moment it is collected until it is assayed. Do not use grossly hemolytic, icteric or lipemic specimens. Samples appearing turbid should be centrifuged before testing to remove any particulate material.

HMGB1 level may increase due to cytolysis, if the centrifugation is not sufficient or the serum/plasma is in contact with blood cells for a considerable period time.

It should be considered that the following criteria may introduce a bias into measured HMGB1 level: age, gender, ethnicity, underlying diseases or health status e.g. smoking.

Sample Collection Device

No special requirements.

Specimen storage

Samples can be stored at 2 - 8°C for 7 days.

It is recommended to freeze samples and store at -80°C for long time storage (< 6 months).

Avoid repeated freeze-thaw cycles. Keep away from heat or direct sunlight.

7. MATERIALS SUPPLIED

Quantity	Symbol	Component
1 x 12x8	MTP	**Microtiter Plate** Coated with antibodies against HMGB1 (monoclonal)
1 x 3.0 mL	CAL CONC	**Standard** Concentrate Contains: HMGB1 (pig) 80 ng/mL
1 x 3.0 mL	CONTROL CONC	**Control** Concentrate Contains: HMGB1 (pig) Concentrations / acceptable ranges see QC certificate.
1 x 100 mL	DILBUF	**Diluent Buffer** Ready to use. Contains: Buffer, 0.01 % NaN_3.
1 x	ENZCONJ LYO	Enzyme Conjugate, lyophilized Contains: Anti-HMGB1,2 antibody (monoclonal) conjugated to peroxidase. Reconstitution volume: 12 mL
1 x 12 mL	ENZCONJDIL	**Enzyme Conjugate Diluent** Ready to use.
1 x 6 mL	COLREA A	**Colour reagent** Ready to use. Contains: TMB
1 x 6 mL	COLREA B	**Colour reagent** Ready to use. Contains: hydrogen peroxide
1 x 12 mL	STOP	**Colour Stop Solution** Ready to use. Contains: 0.35 M H_2SO_4.
2 x 100 mL	WASHBUF CONC	**Wash Buffer** Concentrate (5x) Contains: phosphate buffer, <0.5 %Tween 20.
2 x	FOIL	Adhesive Foil

8. MATERIALS REQUIRED BUT NOT SUPPLIED

1. Micropipettes (Multipette Eppendorf or similar devices, < 3 % CV).
   Volume: 0 - 20µL; 10 - 100µL; 100 - 1000 µL
2. Vortex mixer
3. Wash bottle, automated or semi-automated microtiter plate washing system
4. Bidistilled or deionised water
5. Paper towels, pipette tips and timer
6. Microtiter plate reader capable of reading absorbance at 450 nm (reference wavelength 600 - 650 nm)
7. Polystyrene (PS) or polypropylene (PP) tubes for standard and sample dilution
8. 8-Channel Micropipette with reagent reservoirs
9. Incubator +37°C

9. PROCEDURE NOTES

1. Any improper handling of samples or modification of the test procedure may influence the results. The indicated pipetting volumes, incubation times, temperatures and pre-treatment steps have to be performed strictly according to the instructions. Use calibrated pipettes and devices only.
2. Once the test has been started, all steps should be completed without interruption. Make sure that required reagents, materials and devices are prepared ready at the appropriate time. Allow all reagents and specimens to reach room temperature (18 - 25°C) and gently swirl each vial of liquid reagent and sample before use. Mix reagents without foaming.
3. Avoid contamination of reagents, pipettes and wells/tubes. Use new disposable plastic pipette tips for each component and specimen. Do not interchange caps. Always cap not used vials. Do not reuse wells/tubes or reagents.
4. It is advised to perform duplicate measurements to be able to identify potential pipetting errors.
5. Use a pipetting scheme to verify an appropriate plate layout.
6. Incubation time affects results. All wells should be handled in the same order and time sequences. It is recommended to use an 8-channel Micropipettor for pipetting of solutions in all wells.

7. Microtiter plate washing is important. Improperly washed wells will give erroneous results. It is recommended to use a multichannel pipette or an automatic microtiter plate washing system. Do not allow the wells to dry between incubations. Do not scratch coated wells during rinsing and aspiration. Rinse and fill all reagents with care. While rinsing, check that all wells are filled precisely with Wash Buffer, and that there are no residues in the wells.
8. Humidity affects the coated wells/tubes. Do not open the pouch until it reaches room temperature. Unused wells/tubes should be returned immediately to the resealed pouch including the desiccant.
9. There is no influence in test results by crystal formation in the wells. There is no need to wash the wells before starting the test!
10. Each test run needs a standard curve.

10. PRE-TEST SETUP INSTRUCTIONS

10.1. Preparation of lyophilized or concentrated components

The volumes stated below are for one run with all strips (96 determinations).

Dilute / dissolve	with	Diluent	Storage	Stability
ENZCONJ LYO	12 mL	**ENZCONJDIL CONC**	≤ - 30°C Aliquots (PS or PP tubes)	1 month. Avoid repeated freeze-thaw cycles.

Remarks
1. Add specified amount to the vial.
2. Shake gently by hand for a few seconds. Avoid allowing the solution to contact the rubber stopper as the material may be adsorbed to the rubber.
3. Leave at room temperature for at least 10 min to ensure complete reconstitution.
4. Swirl gently before use. Avoid foaming and contact of the solution and the rubber stopper.

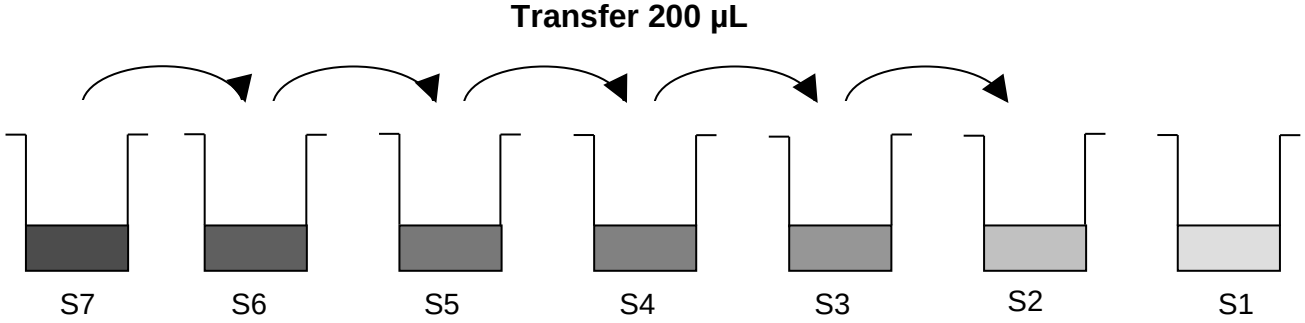
Dilute / dissolve	Component	with	Diluent	Relation	Remarks	Storage	Stability
200 mL	**WASHBUF CONC**	800 mL	bidist. water	1:5	Mix gently, avoid foaming	2 - 25°C	30 days
6 mL	**COLREA A**	6 mL	**COLREA B**	1:2 (1+1)	Prepare immediately before needed.	18 - 25°C	3 hours

10.2. For preparation of standard set.

Label 7 PS or PP tubes, one for each standard point: S7, S6, S5, S4. S3, S2, S1

Dispense a small amount of the concentrated standard (80ng/mL) into tube S7

Pipette 200 µL Diluent Buffer into tubes S6 - S1 and then prepare 1:2 serial dilutions for the standard curve as follows:



Standard	Concentration	Dilution method
7	80 ng/mL	Use Standard as provided.
6	40 ng/mL	Add 200 µL of **Standard 7** to 200 µL of Diluent Buffer and mix.
5	20 ng/mL	Add 200 µL of **Standard 6** to 200 µL of Diluent Buffer and mix.
4	10 ng/mL	Add 200 µL of **Standard 5** to 200 µL of Diluent Buffer and mix.
3	5 ng/mL	Add 200 µL of **Standard 4** to 200 µL of Diluent Buffer and mix.
2	2.5 ng/mL	Add 200 µL of **Standard 3** to 200 µL of Diluent Buffer and mix.
1	0 ng/mL	Use Diluent Buffer as provided.

10.3. Dilution of samples, Standards and Control

Control: Dispense a small amount of the control into a PS or PP tube.

Dilute / dissolve	Component	with	Diluent	Relation	Remarks
10 µL	Samples	400 µL	DILBUF	1:41	Dilute in PS or PP tube.
10 µL	Prepared Standards and Control	400 µL	DILBUF	1:41	Dilute in PS or PP tube. Prepare immediately before needed.

11. TEST PROCEDURE

1.	Pipette **100 µL** of each prediluted **Standard, Control and sample** into the respective wells of microtiter plate.
2.	**Cover** plate with adhesive foil. **Incubate 2 hours** at **+37°C.**
3.	Remove adhesive foil. Discard incubation solution. Wash plate **5 x** with **400 µL** diluted **Wash Buffer**. Remove excess solution by tapping the inverted plate on a paper towel.
4.	Pipette **100 µL Enzyme conjugate** into each well.
5.	Cover plate with adhesive foil. **Incubate 1 hour** at **+25°C.**
6.	Remove adhesive foil. Discard incubation solution. Wash plate **5 x** with **400 µL** diluted **Wash Buffer**. Remove excess solution by tapping the inverted plate on a paper towel.
7.	Note: For adding of Colour solution and Stop solution use, if available, an 8-channel micropipettor. Pipetting should be carried out in the same time intervals for Colour Solution and Stop Solution. Use positive displacement and avoid formation of air bubbles.
8.	Pipette **100 µL** premixed **Colour solution** into each well.
9.	**Incubate 20 min** at **18-25°C** (room temperature) **in the dark.**
10.	Stop the colour reaction by adding **100 µL of Stop solution** into each well. Briefly mix contents by gently shaking the plate.
11.	Clean the back of the wells. Be careful not to scratch the wells as this may interfere with measurements.
12.	Measure optical density with a photometer at **450 nm** (Reference-wavelength: 600-650 nm) within **60 min** after pipetting the Stop Solution.

12. AUTOMATION

Automated protocols can be provided for open ELISA systems: Freedom EVOlyzer®.
For further information please contact: ProductSupport.IBL@tecan.com
Incubation times and conditions can be adapted for optimal automated processing.
For the use of products on automated instruments it is absolutely necessary to perform and maintain a validation according to legal requirements. A successful validation of the process is a prerequisite for diagnostic use. The responsibility for the implementation and documentation of validation in accordance with the country-specific requirements is assumed by the organization or institution.

13. QUALITY CONTROL

The test results are only valid if the test has been performed following the instructions. Moreover, the user must strictly adhere to the rules of GLP (Good Laboratory Practice) or comparable standards/laws. User and/or laboratory must have a validated system to get diagnosis according to GLP. All kit controls must be found within the acceptable ranges as stated on the labels and the QC certificate. If the criteria are not met, the run is not valid and should be repeated. Each laboratory should use known samples as further controls.

In case of any deviation the following technical issues should be proven: Expiration dates of (prepared) reagents, storage conditions, pipettes, devices, incubation conditions and washing methods.

It is recommended to participate at appropriate quality assessment trials.

14. CALCULATION OF RESULTS

The obtained ODs of the standards (y-axis, linear) are plotted against their concentration (x-axis, logarithmic) either on semi-logarithmic graph paper or using an automated method. A good fit is provided with cubic spline, 4 Parameter Logistics or Logit-Log.
For the calculation of the standard curve, apply each signal of the standards (one obvious outlier of duplicates could be omitted and the more plausible single value used).

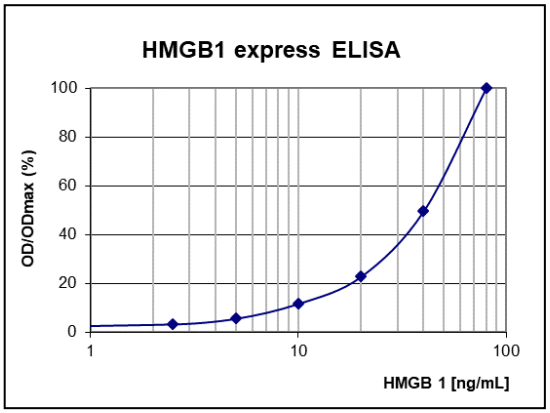
The concentration of the samples can be read directly from the standard curve.

Samples showing concentrations above the highest standard have to be diluted as described in PRE-TEST SETUP INSTRUCTIONS and re-assayed.

In case of diluted samples the values have to be multiplied with the corresponding dilution factor.

Typical Calibration Curve

(Example. Do not use for calculation!)



Standard	HMGB1	OD_{Mean}	OD/OD_{Max}
1	0 ng/mL	0.000	0.0 %
2	2.5 ng/mL	0.052	3.2 %
3	5.0 ng/mL	0.090	5.5 %
4	10 ng/mL	0.191	12 %
5	20 ng/mL	0.374	23 %
6	40 ng/mL	0.818	50 %
7	80 ng/mL	1.650	100 %

Measuring Range: from 1.0 ng/mL (LoQ) to 80 ng/mL (Standard 7)

15. EXPECTED VALUES

The HMGB1 concentration of 53 serum samples from apparently healthy donors of Japanese population were measured in the HMGB1 express ELISA. Reference ranges for EDTA and citrate plasma were transferred from serum by comparison of triplet samples obtained from the same donor.

In an in-house study, apparently healthy subjects showed the following results:

n	Sample (Matrix)	95% Range
53	Serum	0 - 2.9 ng/mL
44	Plasma (EDTA)	0 - 2.2 ng/mL
45	Plasma (Citrate)	0 - 2.7 ng/mL

Method comparison between serum and plasma matrices were analysed by Passing-Bablok regression and resulted in the following equations:

Plasma (EDTA) Concentration (ng/mL) = -1.974 + 1.410 Serum Concentration (ng/mL), r = 0.790

Plasma (Citrate) Concentration (ng/mL) = 0.3291 + 0.788 Serum Concentration (ng/mL), r = 0.884

The results themselves should not be the only reason for any therapeutic consequences. They have to be correlated to other clinical observations and diagnostic tests.

It is recommended that each laboratory establishes its own range of normal values.

16. LIMITATIONS OF THE PROCEDURE

Specimen collection and storage have a significant effect on the test results. See SPECIMEN COLLECTION AND STORAGE for details.
For cross-reactivities, see PERFORMANCE.

	Substance	Concentration
The following substances do not have a significant effect (+/- 20 % of expected value) on the test results up to the stated concentrations	Hemoglobin	500 mg/dL
	Bilirubin	20 mg/dL
	RF	500 IU/mL
	Haptoglobin	120 IU/mL
	Chyle	3000 FTU (Formazine Turbidity Unit)

17. PERFORMANCE

17.1. Analytical Specificity (Cross Reactivity)

Cross-reactivity was tested with pig HMGB2, a compound that could potentially cause interferences in the HMGB1 express ELISA kit. The highest shown cross-reactivity was 6.4 % at a concentration of 160 ng/mL pig HMGB2.

17.2. Evaluation of Detection Capability

Limit of Blank (LoB)

The LoB study was conducted during five days of testing together with the LoD. The runs were performed with a one blank sample and six different low concentrated samples (ranging from 0.25 - 5 ng/mL). Each sample was tested four times. The limit of blank (LoB) was calculated to be 0.39 ng/mL.

Limit of Detection (LoD)

The LoD was determined together with the LoB in the same experiment. See chapter above for the setup of the experiment. The limit of detection (LoD) was calculated to be 0.89ng/mL.

Limit of Quantitation (LoQ)

The LoQ study was determined with CV values obtained by the intra assay reproducibility and was defined as the lowest concentration of HMGB1 quantifiable with CV of 20%. Limit of Quantitation = 1.07 ng/mL.

17.3. Metrological Traceability

The assay HMGB1 express ELISA is metrological traceable to SI units ng/mL by establishment of gravimetrical manufacturing process using purified material with known concentration.

17.4. Linearity

For the linearity study, a dilution linearity experiment was performed. Purified porcine HMGB1 was serially diluted from 100 to 10 ng/mL and 10 to 1 ng/mL.

Concentration range 1 - 80 ng/mL (recovery of expected HMGB1 concentration 94 - 110 %; average: 102%)

17.5. Recovery

The recovery study was performed with five different human serum samples spiked with soluble HMGB1. Each sample (spiked/ not spiked) was measured in duplicate. Measured concentrations of soluble HMGB1 were then compared to the expected values.

The added concentration ranged from 20 - 80 ng/mL.

The mean recovery of HMGB1 from all serum samples was 100.4 ± 3.3 % (range 97.1 - 103.7 %). Measured concentrations did not deviate significantly from the expected concentrations.

17.6. Precision

Intra-assay reproducibility, inter-assay reproducibility and lot-to-lot variation data were determined by repeated measurements on aqueous solutions of purified porcine HMGB1 at various concentrations. The calculated C.V. for lot-to-lot, inter-, and intra-assay variations are below 20 %.

The intra-assay study was conducted by performing different samples in one run. Each sample was tested 20 times.

Sample	n	$Concentration_{mean} \pm SD$	CV
1	20	2.7 ± 0.169 ng/mL	6.2 %
2	20	5.0 ± 0.234 ng/mL	4.7 %
3	20	9.2 ± 0.443 ng/mL	4.8 %
4	20	21.4 ± 0.850 ng/mL	4.0 %
5	20	41.2 ± 1.576 ng/mL	3.8 %
6	20	75.3 ± 2.512 ng/mL	3.3 %

The intra-assay precision showed a mean CV from 4.5 % and a range of 3.3 % - 6.2 %

The inter-assay precision was conducted by performing different samples in 10 independent runs. All samples were measured in duplicates.

Sample	n	$Concentration_{mean} \pm SD$	CV
1	10	6.5 ± 0.38 ng/mL	5.9 %
2	10	74.6 ± 1.94 ng/mL	2.6 %
3	10	22.3 ± 1.008 ng/mL	4.5 %

The inter-assay precision showed an mean CV from 4.3 % and a range between 2.6 - 5.9 %.

The between lot study was conducted by performing different samples with three different kit lots in independent runs.

Sample	n	$Concentration_{mean} \pm SD$	CV
1	3	22.2 ± 0.416 ng/mL	1.9 %
2	3	2.1 ± 0.141 ng/mL	6.6 %
3	3	34.1 ± 0.816 ng/mL	2.4 %

The inter lot precision showed an mean CV from 3.6% and a range between 1.9 - 6.6 %.

18. PRODUCT LITERATURE REFERENCES

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Symbols / Symbole / Symboles / Símbolos / Simboli / Símbolos / Σύμβολα

REF	Cat.-No.: / Kat.-Nr.: / No.- Cat.: / Cat.-No.: / N.–Cat.: / N.º Cat.: / Αριθμός-Κατ.:
LOT	Lot-No.: / Chargen-Bez.: / No. Lot: / Lot-No.: / Lotto n.: / Lote N.º: / Αριθμός -Παραγωγή:
	Use by: / Verwendbar bis: / Utiliser à: / Usado por: / Da utilizzare entro:/ Usar até: / Χρησιμοποιείται από:
Σ	No. of Tests: / Kitgröße: / Nb. de Tests: / No. de Determ.: / Quantità dei tests: / N.º de Testes: / Αριθμός εξετάσεων:
CONC	Concentrate / Konzentrat / Concentré / Concentrar / Concentrato / Concentrado / Συμπύκνωμα
LYO	Lyophilized / Lyophilisat / Lyophilisé / Liofilizado / Liofilizzato / Liofilizado / Λυοφιλιασμένο
IVD	In Vitro Diagnostic Medical Device / In-vitro-Diagnostikum / Appareil Médical pour Diagnostics In Vitro / Dispositivo Médico para Diagnóstico In Vitro / Dispositivo Medico Diagnostico In vitro / Equipamento Médico de Diagnóstico In Vitro / Ιατρική συσκευή για In-Vitro Διάγνωση
BIO	Contains biological material of human origin / Enthält biologisches Material menschlichen Ursprungs / Contient une substance biologique d'origine humaine / Contiene material biológico de origen humano / Contiene materiale biologico di origine umana / Contém material biológico de origem humana / Περιέχει βιολογικό υλικό ανθρώπινης προέλευσης
BIO	Contains biological material of animal origin / Enthält biologisches Material tierischen Ursprungs / Contient une substance biologique d'origine animale / Contiene material biológico de origen animal / Contiene materiale biologico di origine animale / Contém material biológico de origem animal / Περιέχει βιολογικό υλικό ζωικής προέλευσης
UDI	Unique Device Identification / Eindeutige Gerätekennung / Identifiant de dispositif unique / Identificación única de producto / Identificatore univoco del dispositivo / Identificador de dispositivo único / Μοναδικός αναγνωριστικός κωδικός προϊόντος
	Read instructions before use / Arbeitsanleitung lesen / Lire la fiche technique avant emploi / Lea las instrucciones antes de usar / Leggere le istruzioni prima dell'uso / Ler as instruções antes de usar / Διαβάστε τις οδηγίες πριν την χρήση
	Keep away from heat or direct sun light / Vor Hitze und direkter Sonneneinstrahlung schützen / Garder à l'abri de la chaleur et de toute exposition lumineuse / Manténgase alejado del calor o la luz solar directa / Non esporre ai raggi solari / Manter longe do calor ou luz solar directa / Να φυλάσσεται μακριά από θερμότητα και άμεση επαφή με το φως του ηλίου
	Store at: / Lagern bei: / Stocker à: / Almacene a: / Armazenar a: / Conservare a: / Armazenar em: / Αποθήκευση στους:
2-8°C	Store at: 2 - 8°C / Lagern bei: 2 - 8°C / Stocker à: 2 - 8°C / Almacene a: 2 - 8°C / Armazenar a: 2 - 8°C / Conservare a: 2-8°C / Armazenar em: 2-8°C / Αποθήκευση στους: 2-8°C
	Manufacturer: / Hersteller: / Fabricant: / Productor: / Fabricante: / Fabbricante: / Παραγωγός:
	Distributor: / Distributor: / Distributeur: / Distributor: / Distributore: / Distribuidor: / Διανομέας:
	Caution! / Vorsicht! / Attention! / ¡Precaución! / Attenzione! / Cuidado! / Προσοχή!
	Symbols of the kit components see MATERIALS SUPPLIED. Die Symbole der Komponenten sind im Kapitel KOMPONENTEN DES KITS beschrieben. Voir MATERIEL FOURNI pour les symbôles des composants du kit. Símbolos de los componentes del juego de reactivos, vea MATERIALES SUMINISTRADOS. Per i simboli dei componenti del kit si veda COMPONENTI DEL KIT. Para símbolos dos componentes do kit ver MATERIAIS FORNECIDOS. Για τα σύμβολα των συστατικών του κιτ συμβουλευτείτε το ΠΑΡΕΧΟΜΕΝΑ ΥΛΙΚΑ.

Generic table, not all symbols are present in the product

COMPLAINTS: Complaints may be submitted initially written or vocal. Subsequently they need to be filed including the test performance and results in writing in case of analytical reasons.

WARRANTY: The product is warranted to be free from material defects within the specific shelf life and to comply with product specifications delivered with the product. The product must be used according to the Intended use, all instructions given in the instructions for use and within the product specific shelf life. Any modification of the test procedure or exchange or mixing of components of different lots could negatively affect the results. These cases invalidate any claim for replacement.

LIMITATION OF LIABILITY: IN ALL CIRCUMSTANCES THE EXTENT OF MANUFACTURER'S LIABILITY IS LIMITED TO THE PURCHASE PRICE OF THE KIT(S) IN QUESTION. IN NO EVENT SHALL MANUFACTURER BE LIABLE FOR ANY INCIDENTAL OR CONSEQUENTIAL DAMAGES, INCLUDING DAMAGES FOR LOST PROFITS, LOST SALES, INJURY TO PERSON OR PROPERTY OR ANY OTHER INCIDENTAL OR CONSEQUENTIAL LOSS.

The labelling of hazardous substances is according to European directive.
For further country-specific classifications, please refer to the corresponding safety data sheet.

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