WHO Prequalification of In Vitro Diagnostics
PUBLIC REPORT

Product: Monolisa HCV Ag-Ab ULTRA V2
WHO reference number: PQDx 0229-031-00

Monolisa HCV Ag-Ab ULTRA V2 with product codes **72561 and 72562**, manufactured by **Bio-Rad**, **CE-marked regulatory version**, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 24 January 2020.

Summary of WHO prequalification assessment for Monolisa HCV Ag-Ab ULTRA V2

	Date	Outcome
PQ listing	24-Jan-2020	listed
Dossier review	N/A	MR
Site inspection of quality management system	4-6-Apr-2018	MR
Product performance evaluation	1st quarter of 2017	MR

MR: Meets requirements
N/A: Not applicable

Intended use:

According to the claim of intended use from Bio-Rad "*Monolisa HCV Ag-Ab ULTRA V2 is a qualitative enzyme immunoassay that is intended for use as both an aid for diagnosis and as a donor screening test to detect hepatitis C virus capsid and antibodies to hepatitis C virus in human plasma and serum specimens from individual patients and blood donors. The test is intended for use in a laboratory setting by trained laboratory professionals*".

Assay description:

According to the claim of assay description from Bio-Rad, "*Monolisa HCV Ag-Ab ULTRA V2 is based on the use of a solid phase coated with purified HCV antigens: two recombinant proteins from the non-structural region (NS3 and NS4) and a peptide from the structural region (capsid) of the hepatitis C virus, and a monoclonal antibody against the hepatitis C capsid. The liquid phase comprises two conjugates. The first conjugate (R6) consists of a biotinylated monoclonal mouse antibody against the hepatitis C capsid. This monoclonal antibody does not react against the capsid peptide used in the solid phase. The second conjugate (R7) is a mixture of peroxidase-labeled mouse anti-human IgG antibodies and peroxidase-labeled streptavidin.*

The assay procedure includes the following reaction steps:
1) Conjugate 1 and specimens to be tested and the control sera are transferred into the wells of the microplate using calibrated pipette. If antibodies to HCV are present, they will bind to the antigens coated on the solid phase. If hepatitis C capsid antigen is present, this antigen will be bound by the monoclonal antibodies coated on the solid phase and the biotinylated monoclonal antibodies against the capsid hepatitis C antigen (conjugate 1).
2) After incubation at 37°C for 90 minutes and a washing step, the conjugate 2 containing peroxidase-labeled anti-human IgG antibodies and peroxidase-labeled streptavidin are added to each well of the microplate. If human IgG is present, having reacted with the coated antigen on the solid phase, the anti-human IgG conjugate binds to the human antibodies. The conjugated peroxidase/streptavidin binds to the biotin of conjugate 1 if a HCV capsid antigen is present in the specimen.
3) After 30 minutes of incubation at 37°C, the unbound enzymatic conjugate is removed by washing step and the presence of the antigen-antibody-peroxidase complexes are detected by adding the substrate.
4) After 30 minutes of incubation at room temperature (18 - 30°C) and once the reaction has been stopped, the spectrophotometer reading is taken at 450/620-700 nm. The absorbance measured for a specimen allows detection of the presence or absence of HCV antibodies and/or capsid antigens of the hepatitis C in the specimen. The colour intensity is proportional to the quantity of HCV antibodies and/or the hepatitis C capsid antigen bound on the solid phase".

Test kit contents:

Component	**96 tests (product code 72561)**	**480 tests (product code 72562)**
R1 MICROPLATE: 12 strips of 8 wells each, coated with monoclonal anti-capsid antibody of the VHC, purified recombinant hepatitis C antigens (NS3, NS4) and a HCV capsid peptide	1 plate	5 plates
R2 CONCENTRATED WASHING SOLUTION (20X): Tris NaCl buffer pH 7.4 Preservative: ProClin 300 (0.04%)	1 vial × 70 ml	1 vial × 235 ml
R3 NEGATIVE CONTROL: Tris HCl Buffer, containing BSA (Bovine Serum Albumin); Preservative: ProClin 300 (0.1%)	1 vial × 1 ml	1 vial × 1 ml
R4 POSITIVE CONTROL: Human serum containing antibodies to HCV, negative for HBs antigen and for anti HIV-1 and anti HIV-2 antibodies diluted in a Tris HCl	1 vial × 1.5 ml	1 vial × 3 ml

buffer containing BSA, and photochemically inactivated. Preservative: ProClin 300 (0.1%)		
R5a ANTIGEN POSITIVE CONTROL: Antigen positive control synthetic containing a lyophilized capsid peptide.	1 vial × *q.s. ad* 1 ml	1 vial × *q.s. ad* 1 ml
R5b ANTIGEN DILUENT: Distilled water containing a preservative: ProClin 300 (0.5 %)	1 vial × 1 ml	1 vial × 1 ml
R6 CONJUGATE 1: Mouse biotinilated monoclonal antibodies against capsid HCV antigen. Purple coloured Preservative: Sodium azide (< 0.1%), Cosmocil CQ (0.025%)	1 vial × 15 ml	2 vials × 30 ml
R7 CONJUGATE 2: Mouse antibodies directed against human IgG/peroxidase and streptavidin/peroxidase. Green colour. Preservative: ProClin 300 (0.5 %)	1 vial × 15 ml	2 vials × 30 ml
R8 SUBSTRATE BUFFER: Citric acid and sodium acetate solution, pH 4.0, containing H2O2 (0.015%) and dimethyl sulfoxide (DMSO) 4%	1 vial × 60 ml	2 vials × 60 ml
R9 CHROMOGEN - TMB SOLUTION (11X): Solution containing 3.3', 5.5' tetramethylbenzidine (TMB)	1 vial × 5 ml	2 vials × 5 ml
R10 STOPPING SOLUTION: Sulphuric acid solution (H_2SO_4 1N)	1 vial × 28 ml	3 vials × 28 ml
INSTRUCTIONS FOR USE	1	1

Items required but not provided:

Item
Consumables: • Distilled water • Sodium hypochlorite (household bleach) and sodium bicarbonate. • Absorbent paper • Adhesive films • Disposable gloves • Disposable tubes
Durables: • Safety glasses • Graduated cylinders of 10 ml, 200 ml and 1,000 ml
Equipment: • Calibrated automatic or semiautomatic, adjustable or preset pipettes or multipipettes to measure and dispense 50 µl, 80 µl, 100 µl, 200 µl and 1 ml • Vortex mixer • Automatic, semi-automatic or manual microplate washing system • Water-bath, or equivalent microplate incubator, thermostatically set at 37°C ± 1°C (*) • Container for biohazardous waste • Microplate reader equipped with 450, 490 nm and 620-700 nm filters (*) *(*) Consult manufacturer for detailed information about the equipment recommended by our technical department.*

Storage:
The test kit should be stored at 2-8°C.

Shelf-life upon manufacture:
12 months.

Warnings/limitations:
Refer to current version of instructions for use.

Prioritization for prequalification
Based on the established eligibility criteria, Monolisa HCV Ag-Ab ULTRA V2 was given priority for WHO prequalification assessment.

Product dossier assessment

In accordance with the WHO procedure for abbreviated prequalification assessment, Bio-Rad was not required to submit a product dossier for Monolisa HCV Ag-Ab ULTRA V2 as per the "Instructions for compilation of a product dossier" (PQDx_018 v1). Notwithstanding, certain aspects of the product dossier previously submitted for stringent regulatory review were reviewed by an assessor during the site inspection.

However, a review of the instructions for use (IFU) from a technical viewpoint was made and it was noted that human specimens utilised as positive and negative control specimens had not been screened by state of the art methods (nucleic acid detection assays). Bio-Rad are required to introduce screening using more sensitive methods to assure that the use of the control material represents minimum risk to users.

In addition, results of testing for analytical sensitivity were inappropriately aggregated, giving a potentially incorrect impression of the performance of the assay. Bio-Rad have committed to provide the table below, comprised appropriately of the disaggregated data, in the next version of the instructions for use. The intended use of the product was not clearly documented in the IFU to state the clinical indication and use of the test, the testing population for which the intended use and function is for, the intended use setting and intended users. On test limitations, to include other suitable methods for screening and diagnosis of HCV viremic infection.

Commitments for prequalification:

1. Bio-Rad to revise the IFU to include a table of results of analytical specificity, intended use statement and other methods for screening and diagnosis of HCV viraemic infection as stated above. This will be implemented in the next revision of the IFU by 31 October 2023.
2. Bio-Rad to implement requirements of Technical Specification Series for submission to WHO Prequalification-8 (TSS-8)- Immunoassays to detection hepatitis C antibody and/or antigen by 24 January 2023.

Manufacturing site inspection

In accordance with the WHO procedure for abbreviated prequalification assessment, a shortened inspection with fewer inspectors was conducted at the site(s) of manufacture (3, bd Raymond Poincaré, 92430, Marne La Coquette, France and Route de Cassel, 59114, Steenvoorde, France) of Monolisa HCV Ag-Ab ULTRA V2 in 4-6 April 2018 as per the "*Information for manufacturers on prequalification inspection procedures for the sites of manufacture of diagnostics*" (PQDx_014 v4).
The inspection found that the manufacturer had an acceptable quality management system and acceptable manufacturing practices in place that ensured the consistent manufacture of a product of adequate quality.

The manufacturer's responses to the nonconformities found at the time of the inspection were accepted 9 October 2018.
A field safety notice (FSCA 03-17 IDD) was issued and came to WHO's notice via the United Kingdom Medicines and Healthcare Products Regulatory Agency (MHRA) related to lowered optical density (OD) readings for the entire microplate, typically towards the end of the product shelf-life. The reported issue could be related to the R6 reagent (Conjugate 1 – Mouse biotinylated monoclonal antibodies against capsid HCV antigen). Bio-rad's correction was to issue certain lots with reduced shelf-life. Bio-Rad's corrective action was to implement additional controls for the selection of the IgG mouse selected in the R6 reagent used in the manufacturing process. WHO has decided that a re-inspection will be necessary to determine that the corrective action has addressed the root cause of the issue.

Based on the inspection team's review of the manufacturer's systems for the Management of Nonconformities and Corrective Actions, as well as the proposed and implemented corrective actions related to the above referenced field safety corrective actions, the inspection team has concluded that: The manufacturer has proposed and implemented corrective actions (with the outstanding commitments noted) that could reasonably be expected to minimise the risk of the repeat of the failure that led to the above mentioned field safety corrective action.
Based on the site inspection and corrective action plan review, the quality management system for Monolisa HCV Ag-Ab ULTRA V2 meets WHO prequalification requirements.

Product performance evaluation

Monolisa HCV Ag-Ab ULTRA V2 (Bio-Rad) was evaluated at the National Reference Laboratory, Melbourne, Australia, on behalf of WHO in the 1st quarter of 2017 using serum and plasma specimens. From this evaluation, we drew the following conclusions:

Monolisa HCV Ag-Ab ULTRA V2 (Bio-Rad) is a qualitative enzyme immunoassay for the detection of antibodies to HCV and HCV capsid antigen in human serum and plasma. A volume of 50µl of specimen is needed to perform the assay. This type of assay requires

laboratory equipment and cannot be performed in laboratories with limited facilities. Reading of the results must be performed with a spectrophotometer.

In this limited performance evaluation on a panel of 483 specimens characterized using a reference algorithm (Murex anti-HCV (version 4.0) [DiaSorin South Africa Ltd.] and Monolisa anti-HCV Plus ; followed by CHIRON RIBA HCV 3.0 Strip Immunoblot Assay or MP Diagnostics HCV Blot 3.0 on initially reactive specimens), we found an initial sensitivity of 100% (95% CI: 97.1% – 99.9%) and an initial specificity of 100% (95% CI: 98.5% – 100%) compared to the reference results. In this study, 0% of the results were recorded as indeterminate. Lot to lot variation was in the acceptable range for all ten dilution panels.

For four seroconversion panels, Monolisa HCV Ag-Ab ULTRA V2 detected on average 0 specimens earlier than the benchmark assay (Murex Anti-HCV (version 4.0)). For the mixed titer panel (ref 0810-0175, SeraCare), Monolisa HCV Ag-Ab ULTRA V2 correctly classified all 16 specimens. For the low titer panel (ref 0810-0192, SeraCare), Monolisa HCV Ag-Ab ULTRA V2 correctly classified all but one of the 11 specimens.

The invalid rate in this evaluation was 0%.

Labelling

1. **Labels**
2. **Instructions for use**[1]

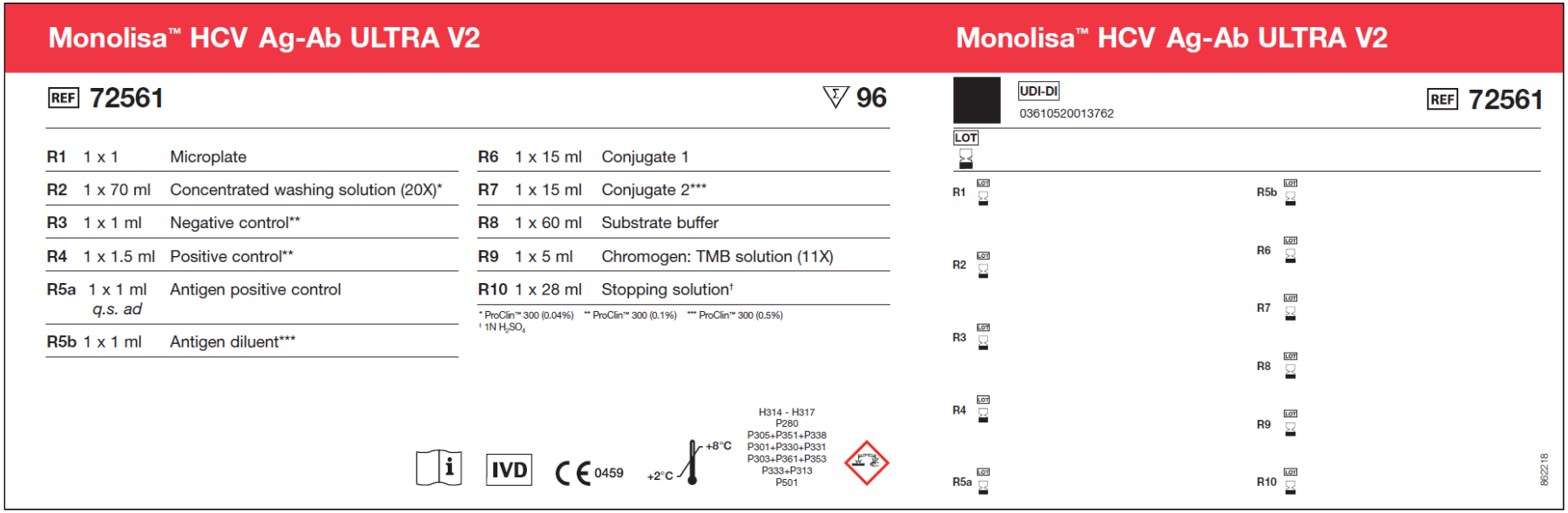
[1] English version of the IFU was the one that was assessed by WHO. It is the responsibility of the manufacturer to ensure correct translation into other languages

1.1 MONOLISATM HCV Ag-Ab ULTRA V2 96 tests - Cat# 72561 Labels

1.1.1: Text printed on the box

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

1.1.2: Box labels



Monolisa™ HCV Ag-Ab ULTRA V2

REF **72561** 96

R1	1 x 1	Microplate	**R6**	1 x 15 ml	Conjugate 1
R2	1 x 70 ml	Concentrated washing solution (20X)*	**R7**	1 x 15 ml	Conjugate 2***
R3	1 x 1 ml	Negative control**	**R8**	1 x 60 ml	Substrate buffer
R4	1 x 1.5 ml	Positive control**	**R9**	1 x 5 ml	Chromogen: TMB solution (11X)
R5a	1 x 1 ml *q.s. ad*	Antigen positive control	**R10**	1 x 28 ml	Stopping solution†
R5b	1 x 1 ml	Antigen diluent***			

* ProClin™ 300 (0.04%) ** ProClin™ 300 (0.1%) *** ProClin™ 300 (0.5%)
† 1N H_2SO_4

IVD CE 0459 +2°C +8°C

H314 - H317
P280
P305+P351+P338
P301+P330+P331
P303+P361+P353
P333+P313
P501

Monolisa™ HCV Ag-Ab ULTRA V2

UDI-DI 03610520013762

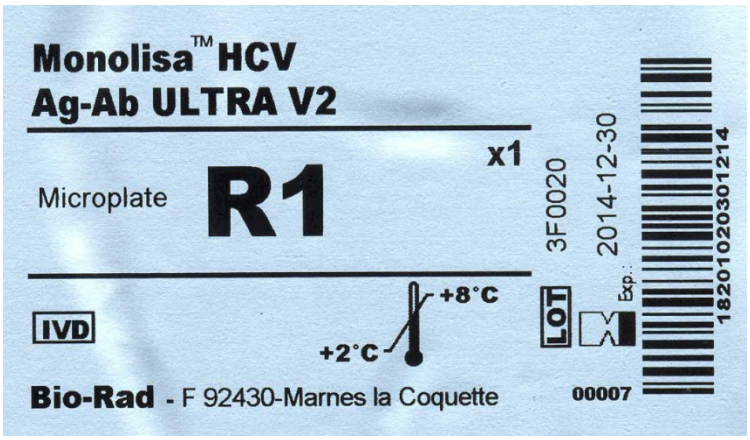
REF **72561**

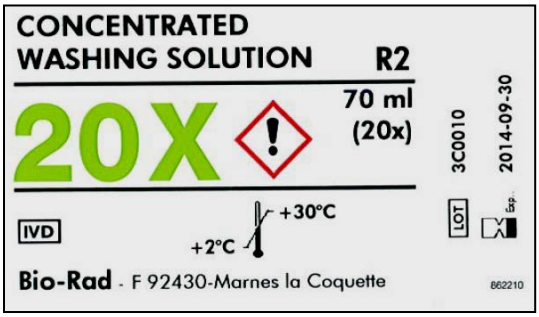
LOT

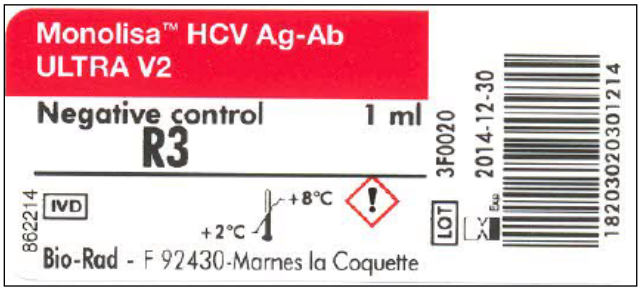
R1 R2 R3 R4 R5a R5b R6 R7 R8 R9 R10

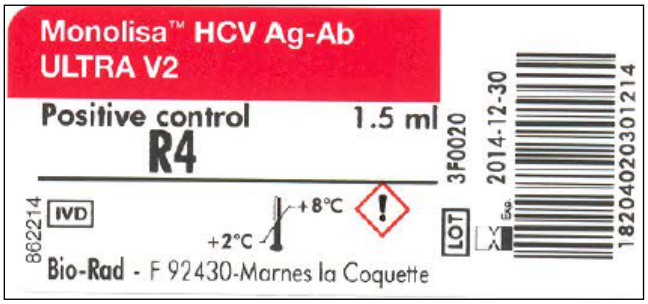
862218

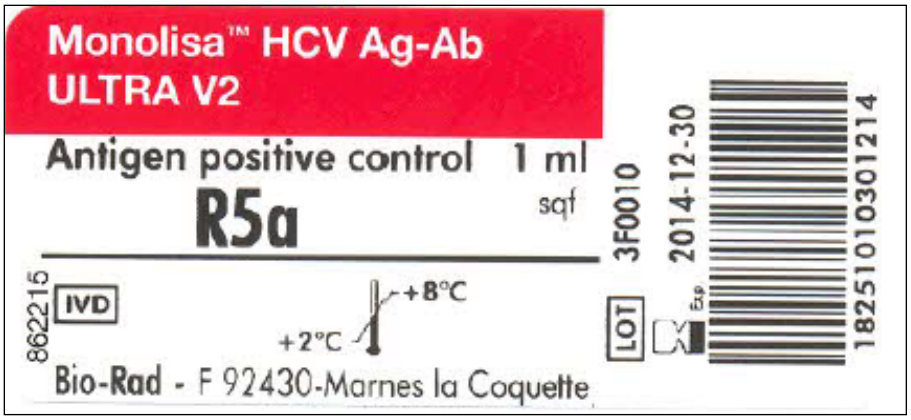
1.1.3: Reagent labels







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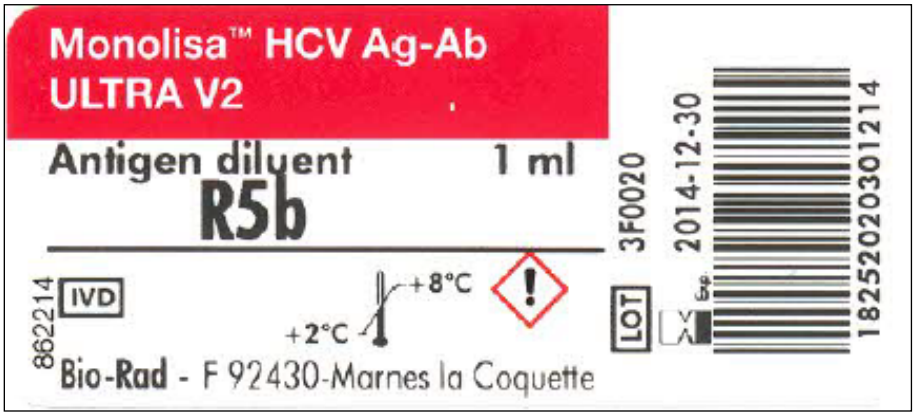
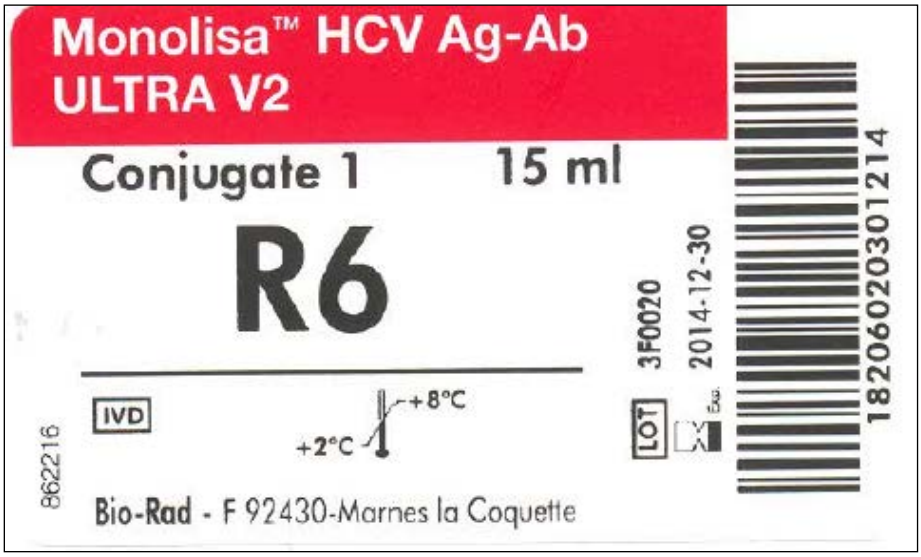
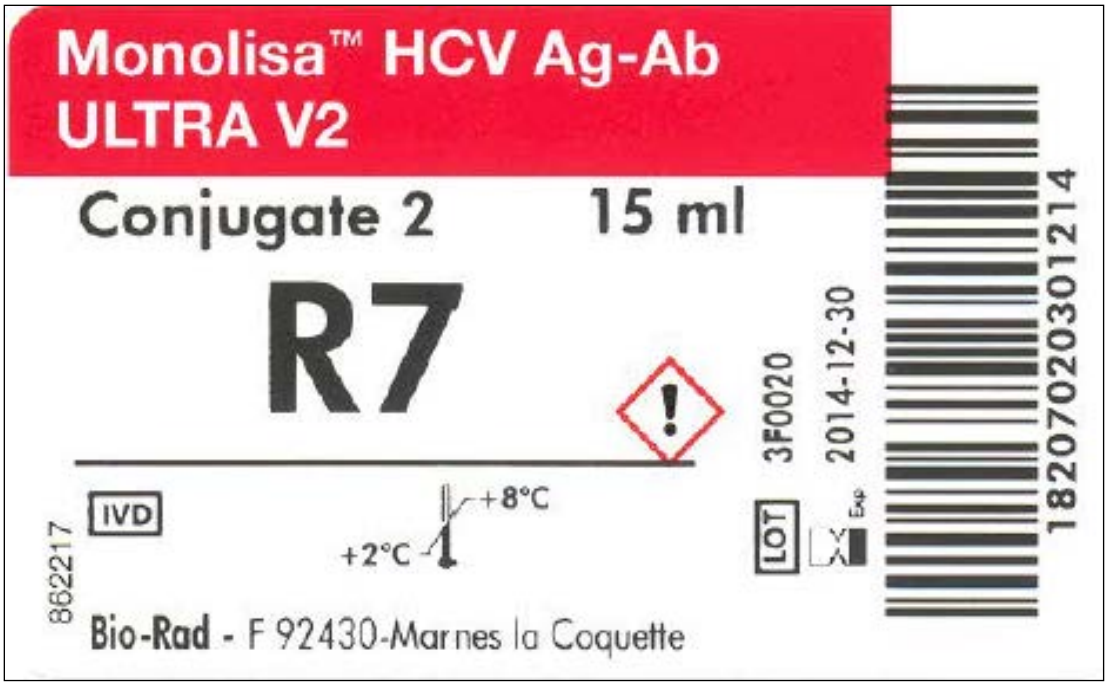
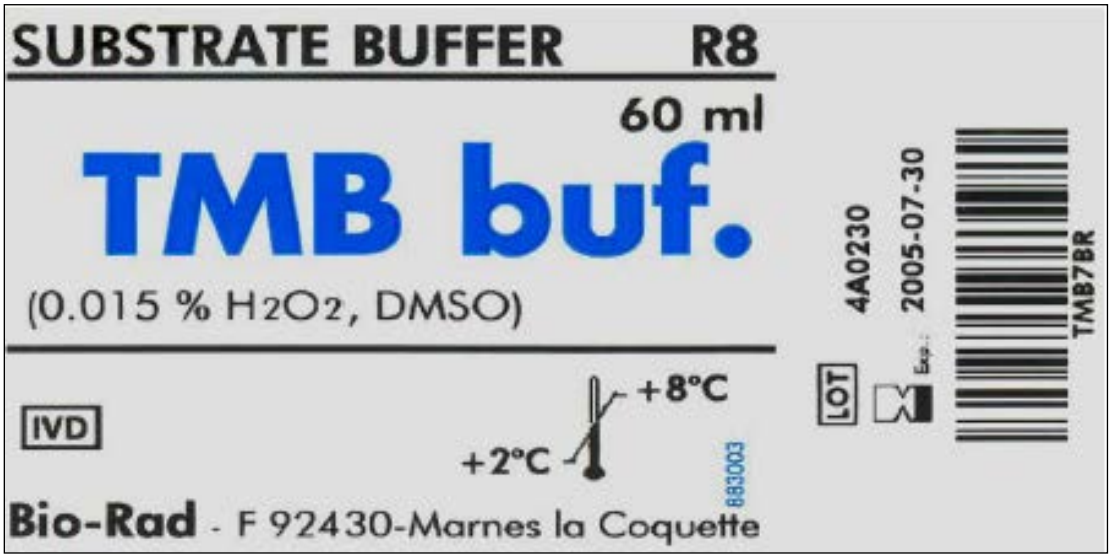
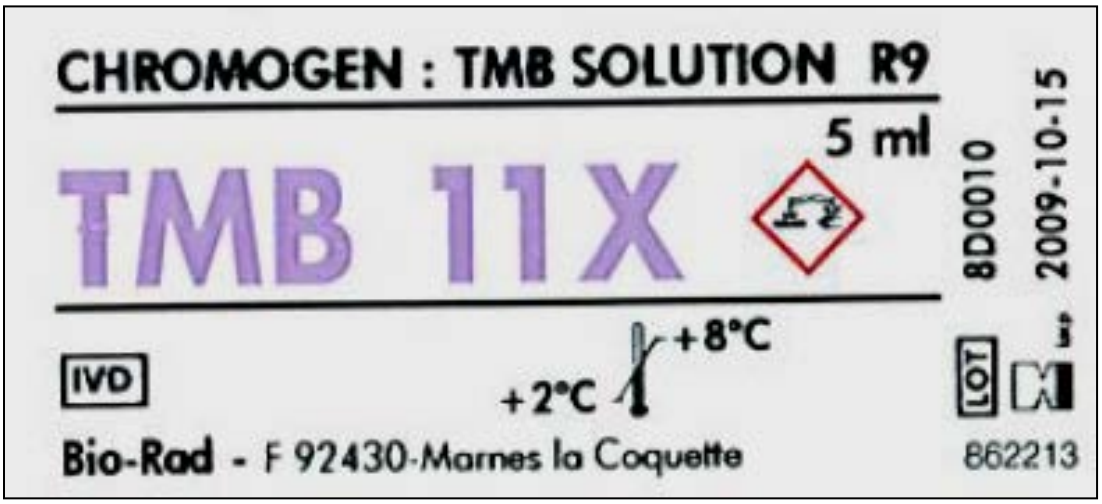
ULTRA V2
Antigen positive control 1 ml
sqf
R5a
862215
IVD
+2°C
+8°C
Bio-Rad - F 92430-Marnes la Coquette
3F0010
2014-12-30
LOT
18251010301214

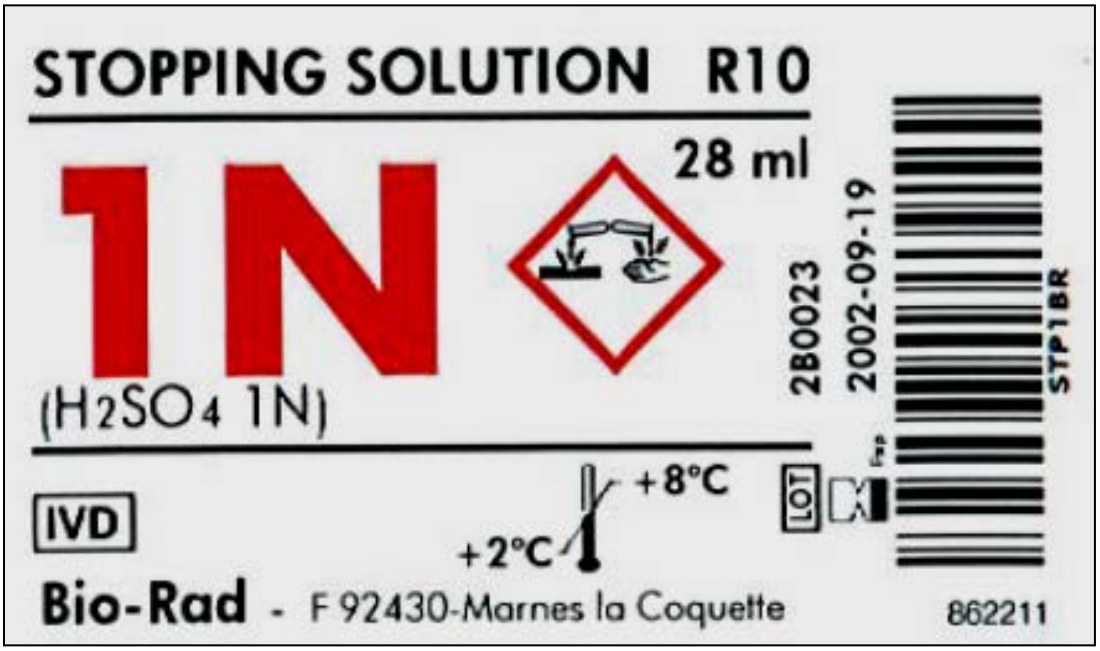

Monolisa™ HCV Ag-Ab
ULTRA V2
Antigen diluent 1 ml
R5b
862214
IVD
+2°C
+8°C
Bio-Rad - F 92430-Marnes la Coquette
3F0020
2014-12-30
LOT
18252020301214


Monolisa™ HCV Ag-Ab
ULTRA V2
Conjugate 1 15 ml
R6
862216
IVD
+2°C
+8°C
Bio-Rad - F 92430-Marnes la Coquette
3F0020
2014-12-30
LOT
18206020301214


Monolisa™ HCV Ag-Ab
ULTRA V2
Conjugate 2
15 ml
R7
IVD
+8°C
+2°C
862217
LOT
3F0020
2014-12-30
Exp
1820702030121 4
Bio-Rad - F 92430-Marnes la Coquette

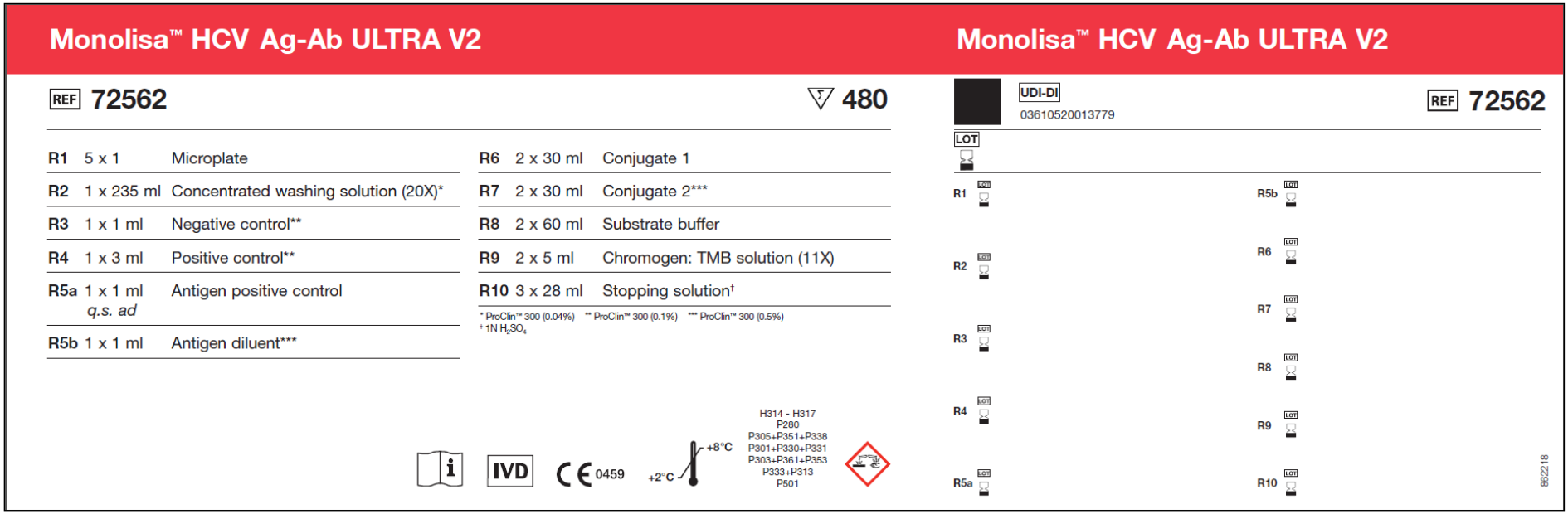

SUBSTRATE BUFFER R8
60 ml
TMB buf.
(0.015 % H2O2, DMSO)
IVD
+8°C
+2°C
883003
LOT
4A0230
Exp
2005-07-30
TMB7BR
Bio-Rad - F 92430-Marnes la Coquette


CHROMOGEN : TMB SOLUTION R9
5 ml
TMB 11X
8D0010
2009-10-15
IVD
+2°C
+8°C
LOT
Bio-Rad - F 92430-Marnes la Coquette
862213

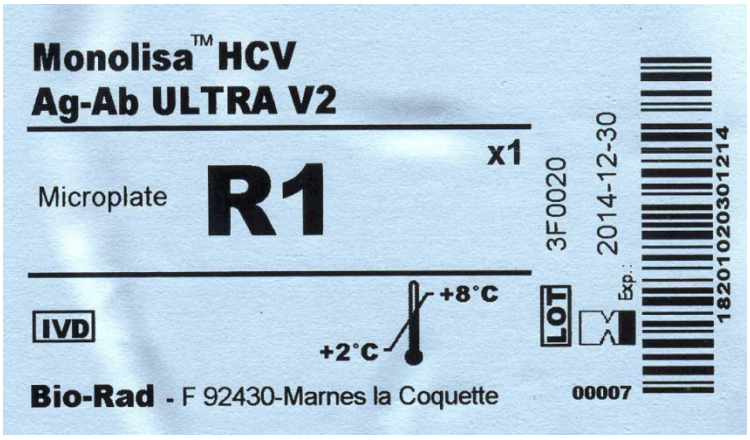

STOPPING SOLUTION R10
28 ml
1N
(H2SO4 1N)
2B0023
2002-09-19
STP1BR
IVD
+2°C
+8°C
LOT
Bio-Rad - F 92430-Marnes la Coquette
862211

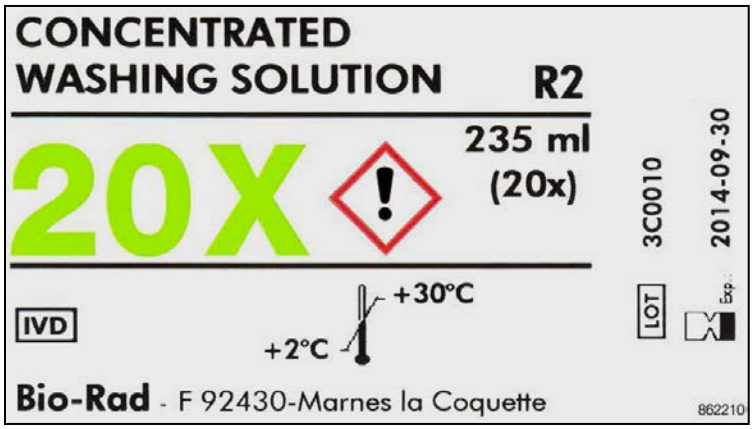
1.2 MONOLISATM HCV Ag-Ab ULTRA V2 480 tests - Cat# 72562

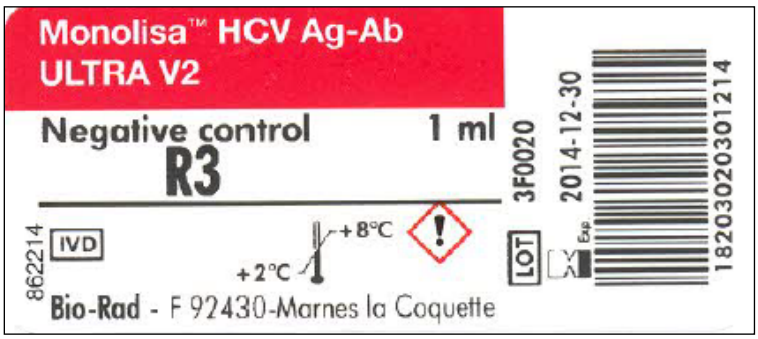
1.2.1: Box labels

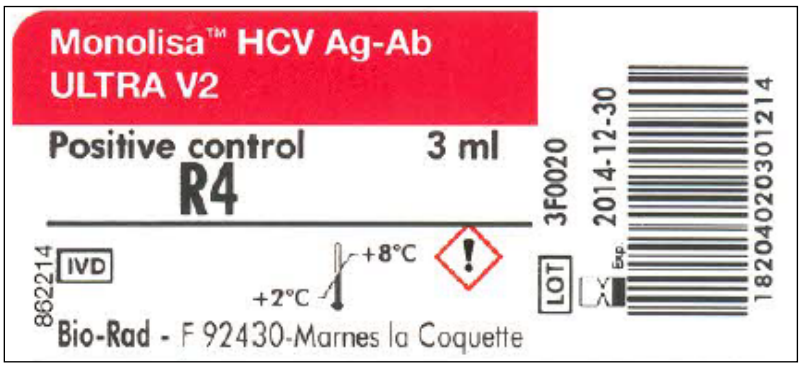


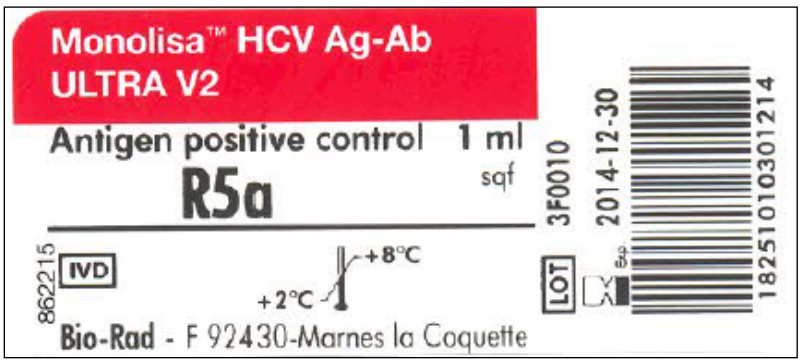
1.2.2 Reagent labels








Monolisa™ HCV Ag-Ab
ULTRA V2
Positive control 3 ml
R4
862214
IVD
+2°C
+8°C
Bio-Rad - F 92430-Marnes la Coquette
LOT
3F0020
2014-12-30
18204020301214


Monolisa™ HCV Ag-Ab
ULTRA V2
Antigen positive control 1 ml
sqf
R5a
862215
IVD
+2°C
+8°C
Bio-Rad - F 92430-Marnes la Coquette
LOT
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2014-12-30
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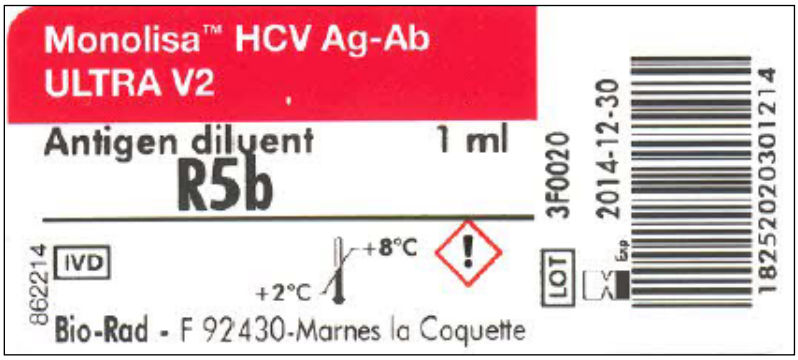
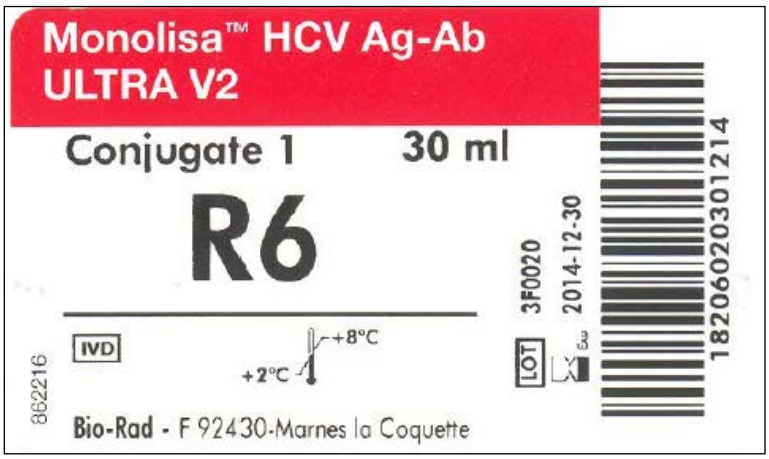

Monolisa™ HCV Ag-Ab
ULTRA V2
Antigen diluent 1 ml
R5b
862214
IVD
+2°C
+8°C
Bio-Rad - F 92430-Marnes la Coquette
LOT
3F0020
2014-12-30
18252020301214


Monolisa™ HCV Ag-Ab
ULTRA V2
Conjugate 1
30 ml
R6
3F0020
2014-12-30
18206020301214
IVD
+8°C
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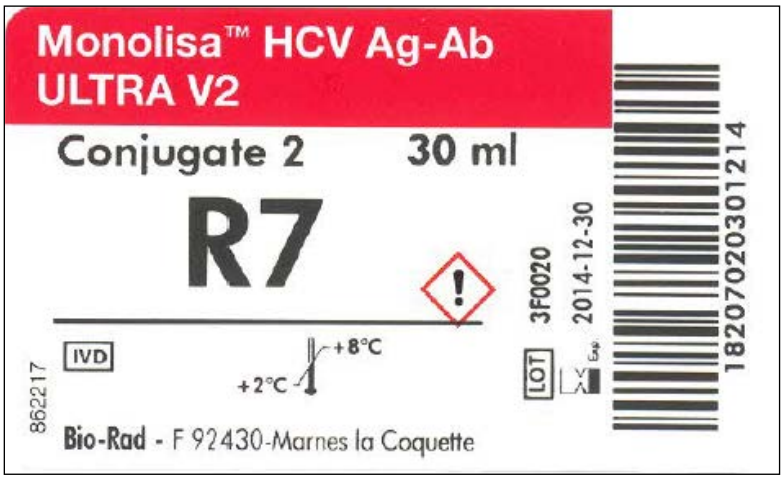
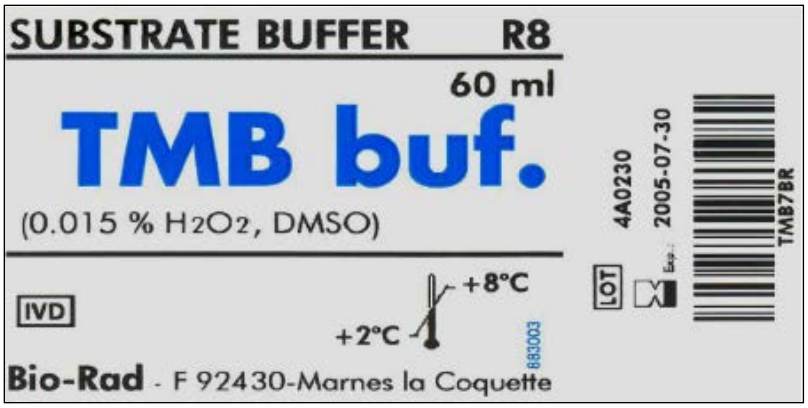
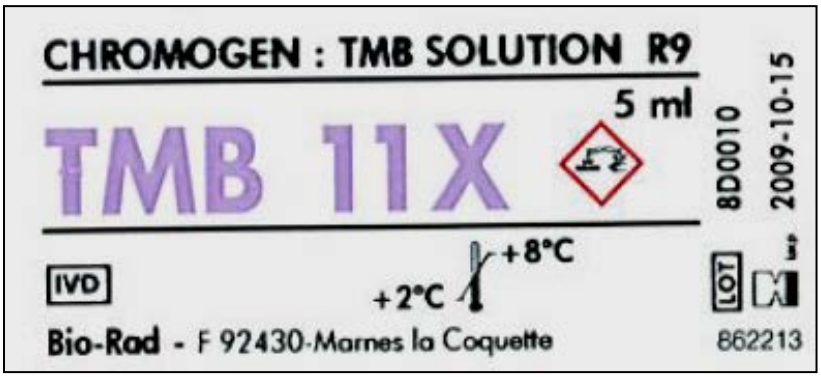
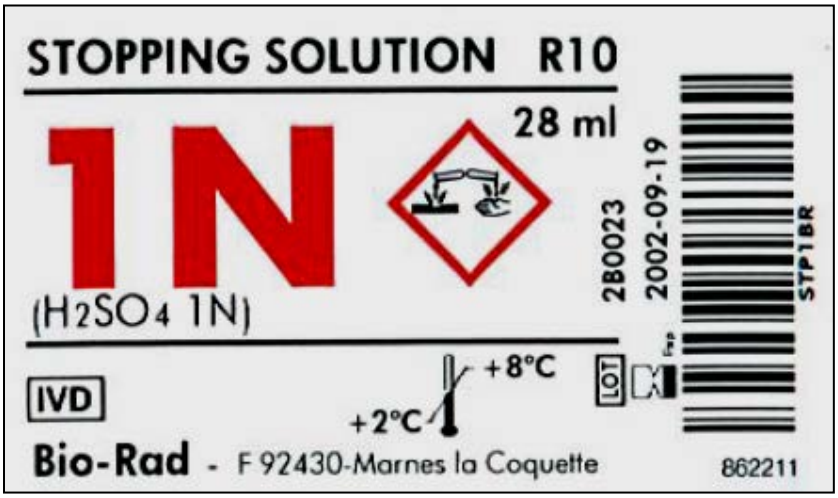
862216
Bio-Rad - F 92430-Marnes la Coquette


Monolisa™ HCV Ag-Ab
ULTRA V2
Conjugate 2
30 ml
R7
3F0020
2014-12-30
18207020301214
IVD
+8°C
+2°C
862217
Bio-Rad - F 92430-Marnes la Coquette


SUBSTRATE BUFFER R8
60 ml
TMB buf.
(0.015 % H2O2, DMSO)
IVD
+8°C
+2°C
883003
Bio-Rad - F 92430-Marnes la Coquette
LOT
4A0230
2005-07-30
TMB7BR


CHROMOGEN : TMB SOLUTION R9
5 ml
TMB 11X
IVD
+8°C
+2°C
Bio-Rad - F 92430-Marnes la Coquette
LOT
8D0010
2009-10-15
862213


STOPPING SOLUTION R10
28 ml
1N
(H2SO4 1N)
IVD
+8°C
+2°C
Bio-Rad - F 92430-Marnes la Coquette
LOT
2B0023
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2. Instructions for use[2]

[2] English version of the IFU was the one that was assessed by WHO. It is the responsibility of the manufacturer to ensure correct translation into other languages

Monolisa™ HCV Ag-Ab ULTRA V2

1 plate - Σ 96 REF 72561
5 plates - Σ 480 REF 72562

(BG) • Други езици можете да получите от представителя на Bio-Rad. Задължително използвайте варианта на листовката, описан върху опаковката (i).

(CZ) • Ostatní požadované jazyky jsou k dispozici u vašeho místního prodejce Bio-Rad. Používejte pouze verzi příbalového letáku uvedenou na obalu (i).

(DE) • Andere Sprachen sind auf Anfrage von Ihrer Bio-Rad-Vertretung vor Ort erhältlich. Es ist zwingend die auf der Schachtel genannte Version der Packungsbeilage zu verwenden (i).

(DK) • Hvis der ønskes andre sprog, kan de fås hos den lokale Bio-Rad-repræsentant. Indlægssedlen, som er angivet på kassen, skal altid anvendes (i).

(EE) • Teistes keeltes juhendi saate soovi korral kohalikult Bio-Rad esindajalt. Kohustuslik on kasutada karbil mainitud pakendi infolehe versiooni (i).

(EN) • Other requested languages can be obtained from your local Bio-Rad agent. Imperatively use the package insert version mentioned on the box (i).

(ES) • Puede solicitar otros idiomas a su agente local Bio-Rad. Utilice obligatoriamente el paquete adjunto, versión indicada en la caja (i).

(FI) • Muita kieliä on saatavilla omalta Bio-Rad -edustajaltanne. Käytä ehdottomasti laatikossa mainittua tuoteselosteversiota (i).

(FR) • Pour obtenir d'autres langues, contacter votre agent Bio-Rad. Utiliser obligatoirement la version de la notice mentionnée sur la boîte (i).

(GR) • Τις άλλες απαιτούμενες γλώσσες μπορείτε να τις πάρετε από τον τοπικό πράκτορά σας Bio-Rad. Χρησιμοποιήστε οπωσδήποτε την παραλλαγή ένθετου συσκευασίας που αναγράφεται στο κουτί (i).

(HR) • Ostali traženi jezici mogu se dobiti od lokalnog Bio-Rad agenta. Potrebno je koristiti onu verziju uputstva za upotrebu koja je navedena na kutiji (i).

(HU) • Egyéb nyelveken a helyi Bio-Rad képviselettől szerezhető be. A dobozon szereplő verziószámú tájékoztatót kell kötelező érvénnyel használni (i).

(IT) • E' possibile avere i Manuali di Istruzioni in altre lingue richiedendoli al collaboratore Bio-Rad di zona. Utilizzare tassativamente il manuale di istruzioni della versione citata sulla confezione (i).

(LT) • Informaciją gimtąja kalba galima gauti iš vietinio „Bio-Rad“ atstovo. Privaloma naudoti įdėtinę paketo versiją, nurodytą ant dėžutės (i).

(MT) • Lingwi oħrajn mitlubin jistgħu jinkisbu mingħand l-aġent ta' Bio-Rad lokali tiegħek. Huwa mistenni li tuża l-verżjoni tal-fuljett ta' tagħrif imsemmija fuq il-kaxxa (i).

(NL) • Andere gevraagde talen kunnen worden verkregen bij uw plaatselijke Bio-Rad agent. Gebruik uitsluitend de op de doos vermelde versie van de bijsluiter (i).

(NO) • Andre etterspurte språk kan fås fra din lokale Bio-Rad representant. Om nødvendig bruk pakningsvedlegget som følger med (i).

(PL) • Informację w innych językach można otrzymać u miejscowego przedstawiciela firmy Bio-Rad. Należy bezwzględnie zapoznać się z ulotką dołączoną do produktu wskazaną na opakowaniu (i).

(PT) • É possível obter outros idiomas solicitados junto da sua agência Bio-Rad local. Consulte obrigatoriamente a versão do folheto informativo referida na embalagem (i).

(RO) • Alte limbi solicitate pot fi obținute de la agentul dumneavoastră local Bio-Rad. Este imperativ să utilizați versiunea prospectului menționată pe cutie (i).

(SE) • Andra språk kan fås av din lokala Bio-Rad-återförsäljare. Använd alltid den version av bipacksedeln som anges på förpackningen (i).

(SI) • Druge želene jezike lahko dobite pri krajevnem zastopniku Bio-Rad. Obvezno uporabite različico navodil za uporabo, navedeno na škatli (i).

(SK) • Ďalšie jazyky si môžete vyžiadať u svojho miestneho zástupcu Bio-Rad. Bezpodmienečne používajte verziu príbalového letáku uvedenú na škatuli (i).

BIO-RAD

Monolisa™ HCV Ag-Ab ULTRA V2

1 plate - Σ 96 REF 72561
5 plates - Σ 480 REF 72562

COMBINED SCREENING KIT FOR ANTI-HCV ANTIBODIES AND THE VIRAL ANTIGEN OF THE HEPATITIS C VIRUS IN SERUM OR HUMAN PLASMA USING AN ENZYME IMMUNOASSAY TECHNIQUE

IVD CE 0459

862224 – 2019/03

CONTENTS

1. INTENDED USE

Monolisa™ HCV Ag-Ab ULTRA V2 is a qualitative enzyme immunoassay that is intended for use as both an aid for diagnosis and as a donor screening test to detect hepatitis C virus capsid and antibodies to hepatitis C virus in human plasma and serum specimens from individual patients and blood donors. The test is intended for use in a laboratory setting by trained laboratory professionals.

2. SUMMARY AND EXPLANATION OF THE TEST

The hepatitis C virus (HCV) is an enveloped RNA positive-sense virus (9.5 kb) belonging to the Flaviviridae family, of which six major genotypes were identified. HCV is recognized as being the main cause of non-A and non-B viral hepatitis. HCV infection is characterized by an acute and chronic disease stages that may lead to liver cirrhosis and hepatocellular carcinoma.
Evidence of HCV infection can be obtained through testing to screen for HCV antigens and/or antibodies in serum or plasma and/or RNA. In comparison to assays for screening for anti-HCV antibodies alone, use of a combined screening assay for both anti-HCV antibodies and the HCV capsid antigen can reduce the serological window period and improve detection of the infection.

3. PRINCIPLES OF THE PROCEDURE

Monolisa™ HCV Ag-Ab ULTRA V2 is based on the use of a solid phase coated with purified HCV antigens: two recombinant proteins from the non-structural region (NS3 and NS4) and a peptide from the structural region (capsid) of the hepatitis C virus, and a monoclonal antibody against the hepatitis C capsid. The liquid phase comprises two conjugates. The first conjugate (R6) consists of a biotinylated monoclonal mouse antibody against the hepatitis C capsid. This monoclonal antibody does not react against the capsid peptide used in the solid phase. The second conjugate (R7) is a mixture of peroxidase-labeled mouse anti-human IgG antibodies and peroxidase-labeled streptavidin.

The assay procedure includes the following reaction steps:

1) Conjugate 1 and specimens to be tested and the control sera are transferred into the wells of the microplate using calibrated pipette. If antibodies to HCV are present, they will bind to the antigens coated on the solid phase. If hepatitis C capsid antigen is present, this antigen will be bound by the monoclonal antibodies coated on the solid phase and the biotinylated monoclonal antibodies against the capsid hepatitis C antigen (conjugate 1).
2) After incubation at 37°C for 90 minutes and a washing step, the conjugate 2 containing peroxidase-labeled anti-human IgG antibodies and peroxidase-labeled streptavidin are added to each well of the microplate. If human IgG is present, having reacted with the coated antigen on the solid phase, the anti-human IgG conjugate binds to the human antibodies. The conjugated peroxidase/streptavidin binds to the biotin of conjugate 1 if a HCV capsid antigen is present in the specimen.
3) After 30 minutes of incubation at 37°C, the unbound enzymatic conjugate is removed by washing step and the presence of the antigen-antibody-peroxidase complexes are detected by adding the substrate.
4) After 30 minutes of incubation at room temperature (18 - 30°C) and once the reaction has been stopped, the spectrophotometer reading is taken at 450/620-700 nm. The absorbance measured for a specimen allows detection of the presence or absence of HCV antibodies and/or capsid antigens of the hepatitis C in the specimen. The colour intensity is proportional to the quantity of HCV antibodies and/or the hepatitis C capsid antigen bound on the solid phase.

4. REAGENTS

4.1. Description

Identification on label		Description	Presentation Preparation 72561	Presentation Preparation 72562
R1	**MICROPLATE**	**Microplate** 12 strips of 8 wells each, coated with monoclonal anti-capsid antibody of the VHC, purified recombinant hepatitis C antigens (NS3, NS4) and a HCV capsid peptide. ***Specific ID number = 93***	1 plate **Ready to use**	5 plates **Ready to use**
R2	**CONCENTRATED WASHING SOLUTION (20X)**	**Concentrated washing solution (20X)** Tris NaCl buffer pH 7.4 Preservative: ProClin™ 300 (0.04%)	1 vial 70 mL **To be diluted**	1 vial 235 mL **To be diluted**
R3	**NEGATIVE CONTROL**	**Negative control** Tris HCl Buffer, containing BSA (Bovine Serum Albumin); Preservative: ProClin™ 300 (0.1%)	1 vial 1 mL **Ready to use**	1 vial 1 mL **Ready to use**
R4	**POSITIVE CONTROL**	**Positive control** Human serum containing antibodies to HCV, negative for HBs antigen and for anti HIV-1 and anti HIV-2 antibodies diluted in a Tris HCl buffer containing BSA, and photochemically inactivated. Preservative: ProClin™ 300 (0.1%)	1 vial 1.5 mL **Ready to use**	1 vial 3 mL **Ready to use**
R5a	**ANTIGEN POSITIVE CONTROL**	**Antigen positive control** Antigen positive control synthetic containing a lyophilized capsid peptide.	1 vial *q.s. ad* 1 mL **To be reconstituted**	1 vial *q.s. ad* 1 mL **To be reconstituted**
R5b	**ANTIGEN DILUENT**	**Diluent of R5a** Distilled water containing a preservative: ProClin™ 300 (0.5 %)	1 vial 1 mL **To be reconstituted**	1 vial 1 mL **To be reconstituted**
R6	**CONJUGATE 1**	**Conjugate 1** Mouse biotinilated monoclonal antibodies against capsid HCV antigen. Purple coloured Preservative: Sodium azide (< 0.1%), Cosmocil® CQ (0.025%)	1 vial 15 mL **Ready to use**	2 vials 2 x 30 mL **Ready to use**
R7	**CONJUGATE 2**	**Conjugate 2** Mouse antibodies directed against human IgG/peroxidase and streptavidin/peroxidase. Green colour. Preservative: ProClin™ 300 (0.5 %)	1 vial 15 mL **Ready to use**	2 vials 2 x 30 mL **Ready to use**
R8	**SUBSTRATE BUFFER**	**Substrate** Citric acid and sodium acetate solution, pH 4.0, containing H_2O_2 (0.015%) and dimethyl sulfoxide (DMSO) 4%	1 vial 60 mL **To be reconstituted**	2 vials 2 x 60 mL **To be reconstituted**
R9	**CHROMOGEN: TMB SOLUTION (11X)**	**Chromogen: TMB solution** Solution containing 3.3', 5.5' tetramethylbenzidine (TMB)	1 vial 5 mL **To be diluted**	2 vials 2 x 5 mL **To be diluted**
R10	**STOPPING SOLUTION**	**Stopping solution** Sulphuric acid solution (H_2SO_4 1N)	1 vial 28 mL **Ready to use**	3 vials 3 x 28 mL **Ready to use**

4.2. Conditions of preservation and handling

The kit should be stored at + (2-8) °C. Each item of the kit preserved at + (2-8) °C can be used up to the expiry date mentioned on the package (unless otherwise indicated).
After opening and in the absence of contamination, the R2, R3, R4, R6, R7, R8, R9 and R10 reagents preserved at (2-8) °C can be used up to the expiry date shown on the label.

Identification	Preservation
R1	After opening the vacuum-sealed bag, the microwell strips stored at +(2-8°C) can be used for 1 month in their carefully resealed original bag with tape. Keep the desiccant inside the original bag after opening
R2	The diluted washing solution can be stored at +(2-30°C) for 2 weeks. The concentrated washing solution (R2) can be stored at +(2-30°C).
R5a + R5b	After reconstitution, the working antigen positive control (R5) solution can be stored for 1 month at +(2-8°C) and 2 months at -20°C (up to 5 freezing/thawing cycles after freezing at -20°C).
R8 + R9	After reconstitution, the reagents stored in the dark can be used within 6 hours at room temperature (18-30°C).

5. WARNING AND PRECAUTIONS

For *in vitro* diagnostic use by a health professional.

5.1. Health and Safety Precautions

- This test kit should be handled only by qualified personnel trained in laboratory procedures and familiar with their potential hazards. Wear appropriate protective clothing, gloves, eye/face protection and handle appropriately with the requisite Good Laboratory Practices.

- The test kit contains human blood components. Human source material used in the preparation of R4 reagent (Positive Control) has been tested and found non-reactive for hepatitis B surface antigen (HBs Ag) and antibodies to Human Immunodeficiency Viruses (HIV-1 and HIV-2 Ab) and positive for anti-HCV antibodies. The positive control R4 is inactivated by warming. No known test method can offer complete assurance that infectious agents are absent. Therefore, all human blood derivatives, reagents and human specimens, should be handled as if capable of transmitting infectious disease, following recommended Universal Precautions for blood borne pathogens as defined by local, regional and national regulations.

- Biological spills: Human source material spills should be treated as potentially infectious.
  Spills not containing acid should be immediately decontaminated, including the spill area, materials and any contaminated surfaces or equipment, with an appropriate chemical disinfectant that is effective for the potential biohazards relative to the specimens involved (commonly a 1:10 dilution of household bleach, 70-80% Ethanol or Isopropanol, an iodophor [such as 0.5% Wescodyne™ Plus, etc.), and wiped dry.
  Spills containing acid should be appropriately absorbed (wiped up) or neutralized, the area flushed with water and wiped dry; materials used to absorb the spill may require biohazardous waste disposal. Then the area should be decontaminated with one of the chemical disinfectants.

NOTE: Do not place solutions containing bleach into the autoclave!

- Dispose of all specimens and material used to perform the test as though they contain an infectious agent. Laboratory, chemical or biohazardous wastes must be handled and discarded in accordance with all local, regional and national regulations.

- For hazard and precaution recommendations related to some chemical components in this test kit, please refer to the pictogram(s) mentioned on the labels and the information supplied at the end of instructions for use. The Safety Data Sheet is available on www.bio-rad.com.

5.2. Precautions relating to the protocol

5.2.1. Preparing

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 reagents from different lots within a test run.
- Before use wait for 30 minutes for the reagents to stabilize at room temperature (18-30°C).
- The name of the test, as well as a specific identification number for the test, is written on the frame of each microplate. This specific identification number is stated on each strip too.

Monolisa™ HCV Ag-Ab ULTRA V2: Specific ID number = 93

Verify the specific identification number before use. If the identification number is missing, or different from the stated number corresponding to the assay to be tested, the strip should not be used.

REMARK: For washing solution (R2, label identification: 20X coloured green), peroxidase substrate buffer (R8, label identification: TMB buffer, coloured blue), chromogen (R9, label identification: TMB 11X, coloured purple) and stopping solution (R10, label identification: 1N coloured red), it is possible to use other lots than those contained in the kit, provided the same lot is used within a given test run. These reagents can be used with some other products of our company. Contact our technical service for detailed information.

- Carefully reconstitute the reagents avoiding any contamination.
- Use glassware thoroughly washed and rinsed with deionized water or preferably, disposable material.
- Do not allow the microplate to dry between the end of the washing operation and the reagent distribution.
- The enzyme reaction is very sensitive to metal ions. Consequently, do not allow any metal element to come into contact with the various conjugate or substrate solutions.
- The development solution (substrate buffer + chromogen) must be coloured pink. The modification of this pink colour within a few minutes after reconstitution indicates that the reagent cannot be used and must be replaced.
  Preparation of the development solution can be made in a clean disposable single use plastic tray or glass container that has first been pre-washed with 1N HCl and rinsed thoroughly with distilled water and dried. This reagent must be stored in the dark.
- Never use the same container to distribute conjugate and development solution.

5.2.2. Processing

- Do not change the assay procedure.
- Do not carry out the test in the presence of reactive vapors (acid, alkaline, aldehyde vapors) or dust that could alter the enzymatic activity of the conjugate.
- Use a new distribution tip for each specimen.
- Well washing is a critical step in this procedure: respect the recommended number of washing cycles and make sure that all wells are completely filled and then completely emptied. Incorrect washing may lead to inaccurate results.
- Carefully follow the washing procedures described to obtain maximum test performance. With some instrument, it could be necessary to optimize the washing procedure (increase of number of cycle of washing step and/or volume of wash buffer for each cycle) to obtain an acceptable level of OD background for the negative specimen.
- Contact our company for the adaptations and special procedures.

6. SPECIMENS

Collect a blood specimen according to the current practices.

Testing should be performed on undiluted serum or plasma (collected on EDTA, Sodium Citrate or ACD). The use of a specimen taken from the tubes containing lithium heparinate as an anticoagulant is not recommended.

1. A lower signal was observed on HCV antigen positive specimens when specimen using this anticoagulant was utilized.
2. Specimens containing aggregates must be clarified by centrifugation before testing. Suspended fibrine particles or aggregates may produce false reactive results.

3. Specimens stored at + (2-8) °C can be used if the test is performed within 7 days of collection. If they will not be used within this time period they should be deep-frozen at -20 °C. Do not repeat more than 3 freeze/thaw cycles. Specimens must be equilibrated at room temperature (18-30°C) before testing. It is recommended to mix them by inverting them before use.

4. Specimens containing up to 120 g/L of albumin, 50 µg/L of biotin, and 200 mg/L of bilirubin, specimens containing up to 33 g/L of triolein and specimens containing up to 2 g/L of hemoglobin do not affect the results. However, it is not recommended to use contaminated hyperlipemic and hyperhemolysed specimens.
5. It is not recommended to heat the specimens because this could significantly reduce detection of the HCV antigen.
6. If the specimens are to be shipped, they must be packaged in accordance with the regulations in force regarding the transport of etiological agents and preferably transport frozen.

7. PROCEDURE

7.1. Materials required but not provided

- Distilled water.
- Sodium hypochlorite (household bleach) and sodium bicarbonate.
- Absorbent paper.
- Adhesive films.
- Disposable gloves.
- Safety glasses.
- Disposable tubes.
- Automatic or semiautomatic, adjustable or preset pipettes or multipipettes to measure and dispense 50 µL, 80 µL, 100 µL, 200 µL and 1 mL.
- Graduated cylinders of 10 ml, 200 ml and 1,000 mL. Vortex mixer.
- Automatic, semi-automatic or manual microplate washing system.
- Water-bath, or equivalent microplate incubator, thermostatically set at 37°C ± 1°C (*).
- Container for biohazardous waste.
- Microplate reader equipped with 450, 490 nm and 620-700 nm filters (*).

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

7.2. Reagents preparation

7.2.1. Ready for use reagents

Reagent 1 (R1): Microplate
Each frame support containing 12 strips is wrapped in a sealed foil bag. Cut the bag using scissors 0.5 to 1 cm above the sealing. Open the bag and take out the frame. Put the unused strips back into the bag. Close the bag carefully with tape and put it back into storage at +(2-8°C).

Reagent 6 (R6): Conjugate 1
Homogenize by inverting before use.

Reagent 7 (R7): Conjugate 2
Homogenize by inverting before use.

7.2.2. Reagents to reconstitute

Reagent 2 (R2): Concentrated washing solution (20X)
Dilute 1:20 in distilled water to obtain the ready-for-use washing solution.
Prepare 800 ml for one plate of 12 strips.

Reagent 8 (R8) + Reagent 9 (R9): Enzyme development solution
Dilute 1:11 the chromogen (R9) in the Substrate Buffer (e.g. 1 ml reagent R9 + 10 ml of R8 reagent) given that 10 ml are necessary and sufficient to treat 12 strips. Homogenize.

Reagent 5a (R5a) + Reagent 5b (R5b): Working solution (R5).
Pour the content of R5b diluent in the lyophilized Ag R5 vial. Recap the vial and let stand for 10 minutes at room temperature (18-30°C) with shacking and inverting vial from time to time to ease dissolution.

7.3. Assay procedure

Strictly follow the procedure.
Use negative and positive control sera for each test in order to validate the test quality.
Follow the following Good Laboratory Practice:

1) Carefully establish the specimen distribution and identification plan.
2) Prepare the diluted washing solution R2 and the antigen positive control working solution (R5a + R5b). (refer to § 7.2)
3) Take out from the protective packing the support frame and the necessary number of strips (R1). Put the unused strips back in their packing. Close the packing and replace it at (+2-8°C).
4) Distribute in the well in the following order (advisable plate distribution):
   - 100 µL of conjugate 1 (R6) in each well then
   - 50 µL of negative control (R3) in well A1,
   - 50 µL of positive control (R4) in wells B1, C1, D1,
   - 50 µL of the working positive control antigen solution (R5a + R5b) in well E1,
   - 50 µL of the first specimen in well F1,
   - 50 µL of the second specimen in G1, etc.

   Homogenize the mixture with at least 3 aspirations or with a microplate shaker for 5 seconds. If the distribution of the specimens takes over 10 minutes, it is recommended to distribute the negative and positive controls after the patient specimens.
   Depending on the system used, it's possible to modify the position of controls or the order of distribution.

REMARK: *After the specimens distribution, the well containing specimen (or controls) turns purple to blue. It is possible to verify the presence of the (specimen + conjugate 1) in the wells by spectrophotometric reading at 620 nm (refer to § 7.7).*

5) When possible cover the plate with new adhesive film.
6) Incubate the microplate for 90 minutes (± 5 min.) at 37°C ± 1°C.
7) If necessary, remove the adhesive film. Aspirate the contents of all the wells in a liquid waste container and add a minimum of 370 µL of washing solution into each well. Aspirate again and repeat the washing a minimum of 5 times. The residual volume must be lower than 10 µL (if necessary, dry the strips by turning them upside down on absorbent paper).
   If you have an automatic washer, follow the same operating cycle.
8) Mix the conjugate 2 (R7) gently before use. Distribute quickly 100 µL the solution of conjugate 2 (R7) into each well within the plate.
   If possible cover with a new adhesive film and incubate for 30 minutes (± 5 min.) at 37°C ± 1°C.

REMARK: The conjugate is coloured green. It is possible to verify the presence of conjugate in the wells by spectrophotometric reading at 620 nm (refer to § 7.7).

9) If necessary remove the adhesive film, empty all the wells by aspiration and wash a minimum of 5 times as described above.
10) Prepare enzymatic development solution (reagent R8 + R9).
11) Quickly distribute 80 µL of prepared enzymatic development solution (R8 + R9) in all the wells. Allow the reaction to develop in the dark for 30 minutes (± 5 min) at room temperature (18 - 30°C). Do not use adhesive film during this incubation.

REMARK: The distribution of the development solution, which is coloured pink, can be visually controlled at this step of the manipulation. There is a clear difference of colouration between an empty well and a well containing the pink substrate solution. (Refer to § 7.7).

12) Add 100 µL of the stopping solution (R10) using the same sequence and same rate of distribution as for the development solution.

REMARK: Distribution of the colourless stopping solution can be visually controlled at this handling stage. The substrate colour, pink (for negative specimens) or blue (for positive specimens), fades from the wells, which become colourless (for negative specimens) or yellow (for positive specimens) after adding stopping solution.

13) Carefully wipe each plate bottom. Wait at least 4 minutes after stopping solution addition and within 30 minutes of stopping the reaction, read the optical density at 450/620-700 nm using a plate reader.
14) Check for agreement between the spectrophotometric and visual readings reading and against the plate and specimen distribution and identification plan.

7.4. Quality control

Use positive controls (R4 and R5) and the negative control (R3) in each run of test to validate the assay. (Refer to §7.5)

7.5. Test validation criteria

This test is validated if the conditions below are respected:

1) **For the negative control R3:**
   The measured absorbance value must be less than 60% of the cut off:
   O.D. < cut off x 0.6

2) **For the antibodies positive control R4:**
   0,800 ≤ Mean O.D. R4 ≤ 2,700
   If one of the positive control R4 individual values differs by more than 30% from the mean value, disregard the value and carry out the calculation again with the two remaining positive control values.

3) **For the working solution R5:**
   O.D. > 0.500

7.6. Calculation/Interpretation of results

The cut-off is determined with the R4 positive control:
Calculate the mean measured absorbance value for the positive control R4.

Calculate the cut off value:

$$CO = \frac{\text{Mean OD R4}}{5}$$

The presence or absence of anti-HCV antibodies and/or HCV capsid antigen is determined by comparing the registered absorbence to the calculated cut-off value for each specimen.

The following ratio is calculated for each specimen:
Ratio = OD of the specimen / CO Value

Specimens with an optical density lower than the cut off value are considered to be negative (ratio < 1) by the Monolisa™ HCV Ag-Ab ULTRA V2.

Results just below the cut-off value (CO-10 % < O.D. < CO, ratio between 0.9 and 1) should however, be interpreted with caution. It is advisable to retest in duplicate the corresponding specimens when the systems and laboratory procedures permit.

Specimens with optical density greater or equal to the cut off (ratio ≥ 1) are considered to be initially positive by the Monolisa™ HCV Ag-Ab ULTRA V2. **They should be retested in duplicate before final interpretation.**

If after retesting the ratio value of at least one of the 2 duplicates is equal to or greater than 1, the initial result is repeatable and the specimen is declared to be positive with the Monolisa™ HCV Ag-Ab ULTRA V2.
The ratio values of the 2 duplicates are less than 1, the initial result is non-repeatable and the specimen is declared to be negative.

The specimens which have been retested twice and found negative with Monolisa™ HCV Ag-Ab ULTRA V2, but with one value near the cut-off value (ratio between 0.9 and 1) should be considered with care. It is advised to retest the patient with another method or on another specimen.
In case of very low optical density for tested specimens (negative OD) and when the presence of specimens as well as of reagent is controlled, the results can be interpreted as negative.

It is recommended to confirm the positive specimens following the current national recommendations and algorithms.

7.7. Spectrophotometric verification of specimens and conjugate pipetting (optional)

Specimen and Conjugate 1 (R6) pipetting verification
It is possible to verify the presence of conjugate 1 (R6) + specimen into the well can be verified by automatic reading at 620 nm.
Each well containing specimen and conjugate 1 (R6) must have an OD greater than 0.800.
REMARK: After specimen addition, conjugate 1 (R6) turns purple to blue.

Conjugate 2 (R7) pipetting verification
The conjugate 2 (R7) is coloured green.
The presence of conjugate 2 (R7) into the wells can be controlled by automatic reading at 620 nm: The OD value of each well must be greater than 0.300 (a value lower than this normally indicates a poor dispensing of the conjugate).

Development solution pipetting verification
It is possible to verify the presence of pink development solution into the well by automatic reading at 490 nm.
A well with development solution must have an optical density greater than 0.100 (a lower OD indicates a poor dispensing of the development solution).
There is a significative colour change for the empty wells from uncoloured to pink after addition of prepared substrate chromogen solution.

8. TEST LIMITATION

Due to the diverse immunological responses of patients infected by the hepatitis C virus (especially during seroconversions), some differences of detection can be observed between tests depending on the type of antigenic proteins used. A negative result during a screening test does not therefore exclude the possibility of exposure to or infection by the hepatitis C virus.
Any ELISA technique may produce false positive reactions.
It is recommended to check the specificity of the reaction of any specimen found to be a repeatedly positive, according to the interpretation criteria of the Monolisa™ HCV Ag-Ab ULTRA V2 kit using suitable methods:
ELISA anti-HCV antibody screening or an immunoblot anti-HCV to confirm the presence of anti-HCV antibodies, and / or quantitative / qualitative NAT for detection of HCV RNA or HCV core antigen assay to diagnose viraemic infection.
According to the literature, HCV carriers undergoing immunosuppression treatment or coinfected with HIV-HCV may have particularly low antibody levels, below the detection limit of the HCV tests.

The colorimetric method to check for the deposition of specimens and/or conjugates and/or the development solution does not allow the accuracy of the distributed volumes to be checked and only reveals the presence of the specimen and/or conjugates and/or the development solution. The rate of wrong answers with this method is closely linked to the accuracy of the utilized system (cumulated coefficient of variation of dispensing and reading above 10% significantly decrease the quality of the verification).
The use of the Monolisa™ HCV Ag-Ab ULTRA V2 test is not approved for pools of specimens or diluted specimens.
Fine particles could be seen exceptionally in the Conjugate 1 (R6), their presence in any case does not alter the quality of the reagent.

9. PERFORMANCES CHARACTERISTICS

9.1. Precision Measurement

The reproducibility and intermediate precision have been determined using specimens with different concentrations of anti-HCV antibodies and HCV antigens. The specimens were tested 30 times during the same series of tests to determine the repeatability.
The intermediate precision has been evaluated by testing the specimens in duplicate during 20 days on 2 independent runs each day.
The ratio means, standard deviations and coefficients of variation (CV) were calculated.

9.1.1. Repeatability

Specimens		N	Mean of ratios	Standard deviation	CV %
Negative	S1	30	0.23	0.024	**10.4**
HCV Antigen Positive	S2	30	1.21	0.048	**4.0**
	S3	30	1.43	0.053	**3.7**
	S6	30	7.18	0.166	**2.3**
Anti-HCV antibodies Positive	S4	30	1.42	0.046	**3.2**
	S5	30	1.35	0.083	**6.1**
	S7	30	6.73	0.153	**2.3**

The CVs obtained on 6 positive specimens were <10%.

9.1.2. Intermediate precision

Specimens		N	Mean of ratios	Intra assay		Inter assay / operator		Inter day		Total reproducibility	
				SD	CV %	SD	CV %	SD	CV %	SD	CV %
Negative	S1	80	0.22	0.017	**7.5**	0.028	**12.5**	0.029	**12.7**	0.043	**19.4**
HCV Antigen Positive	S2bis	80	2.80	0.143	**5.1**	0.277	**9.9**	0.283	**10.1**	0.421	**15.0**
	S3	80	1.56	0.124	**7.9**	0.129	**8.2**	0.083	***5.3***	0.197	**12.6**
	S6	68	6.69	0.500	**7.5**	0.621	**9.3**	0.557	**8.3**	0.973	**14.5**
Anti-HCV antibodies Positive	S4	80	1.57	0.062	**3.9**	0.125	**8.0**	0*	N/A	0.140	**8.9**
	S5	80	1.75	0.075	**4.3**	0.164	**9.3**	0*	N/A	0.181	**10.3**
	S7	80	7.69	0.285	**3.7**	0.531	**6.9**	0*	N/A	0.603	**7.8**

*: The negative variance value is estimated at 0.

The CVs obtained on 6 positive specimens are no more than 15%.

9.2. Clinical performance

The performance of the Monolisa™ HCV Ag-Ab ULTRA V2 has been determined by testing specimens from random blood donors, hospitalized patients, patients with acute and chronic hepatitis C virus infection, and patients with clinical signs unrelated to hepatitis C virus infection. The studies were carried out at 2 blood donor sites, at a hospital site and at the Bio-Rad site.

9.2.1. Diagnostic Specificity

The study was carried out on serum and EDTA plasma specimens collected at 2 donor centers on random donors.
A specificity study was also carried out on specimens from hospitalized patients.
All the specimens were tested with a CE marked anti-HCV serological assay.

Population	Site	Type of specimen	Number	Repeated reactive specimens (RR)	Specificity (%)	Confidence interval 95%
Blood donors	#1	serum	537	1	536/537	
		plasma	2002	0	2002/2002	
	#2	serum	2638	2	2636/2638	
	#1 + #2		**5177**	**3**	**99.94%** 5174/5177	**99.83% – 99.99%**
Hospitalized patients	#3	serum	502	1	**99.80%** 501/502	**98.92% - 100.00%**

*: 3 donors found to be indeterminate with the reference test were removed from the calculations

9.2.2. Diagnostic Sensitivity

The diagnostic sensitivity was studied on 575 specimens from patients infected by the hepatitis C virus. Among these specimens, 25 were collected within 24 hours before analysis. 481 different genotyped specimens (1; 2; 3; 4; 5; 6) were tested.

Table 1: Tested genotypes

Genotypes	***1*** *(1, 1a, 1b, 1a/b)*	***2*** *(2 2a/c, 2a, 2b, 2b/3*	***3*** *(3, 3a, 3b, 3c)*	***4*** *(4, 4a, 4a/c, 4a/c/d, 4c, 4e, 4h, 4n, 4r)*	***5*** *(5, 5a)*	***6*** *(6, 6a, 6a/b, 6n)*	***Total***
N	241	56	107	63	8	6	481

The diagnostic sensitivity over all the tested specimens was 100% (575/575) with a 95% confidence interval of [99.4-100.0].

Specimens from patients with an acute infection:
39 seroconversion panels (10 capsid profiles, 10 NS3 profiles and 19 multiples profiles) were tested with the Monolisa™ HCV Ag-Ab ULTRA V2 assay and compared with a CE marked combined antigen/antibody assay and with a CE-Marked anti-HCV antibody assay. Earliness of detection has been measured for all panels.
Of these 39 panels, one panel was not detected by Monolisa™ HCV Ag-Ab ULTRA V2 and three were not detected by the combined Ag-Ab assay.
On the 38 panels detected by Monolisa™ HCV Ag-Ab ULTRA V2, 5 had an earlier detection, 27 had an equivalent detection and 6 had a later detection compared to the combined Ag-Ab assay. In comparison with an anti-HCV antibody test, 28 panels had an earlier detection, 9 had an equivalent detection and 1 had a later detection.

	Monolisa™ HCV Ag-Ab ULTRA V2 *versus* combined Ag-Ab HCV assay	**Monolisa™ HCV Ag-Ab ULTRA V2 *versus* Anti-HCV assay**
Number of panels	**38**	**38**
Earlier detection	5	28
Equivalent detection	27	9
Later detection	6	1

9.3. Analytical Specificity / cross reactivity study

365 potentially interfering specimens containing antibodies against pathogens that could lead to infectious illnesses were tested with the Monolisa™ HCV Ag-Ab ULTRA V2 assay.
Two specimens were found repeatably positive with the Monolisa™ HCV Ag-Ab ULTRA V2 assay. The specificity observed on this target population of 99.45% (363/365) was similar to the specificity of clinical specimens.

Table: Reactivity of the Monolisa™ HCV Ag-Ab ULTRA V2 in Specimens from individuals with Medical Conditions Unrelated to HCV Infection, and in Specimens Containing Potentially Interfering Substances

Conditions	Monolisa™ HCV Ag-Ab ULTRA V2			
	N	Non reactive	Positive IR	Positive RR
anti HIV antibodies (HIV-1, HIV-2)	10	10	0	0
anti HTLV I/II antibodies	10	10	0	0
anti CMV IgG antibodies	5	5	0	0
anti CMV IgM antibodies	**36**	**35**	**1**	**0**
anti EBV IgG antibodies	5	5	0	0
anti EBV IgM antibodies	5	5	0	0
anti HSV-1 IgG antibodies	5	5	0	0
anti HSV-1 IgM antibodies	5	5	0	0
anti VZV IgG antibodies	5	5	0	0
anti VZV IgM antibodies	5	5	0	0
anti Mumps IgG antibodies	5	5	0	0
anti Mumps IgM antibodies	5	5	0	0
anti Measles IgG antibodies	5	5	0	0
anti Measles IgM antibodies	5	5	0	0
anti Rubella IgG antibodies	5	5	0	0
anti Rubella IgM antibodies	5	5	0	0
anti Toxoplasma gondii IgG antibodies	5	5	0	0
anti Toxoplasma gondii IgM antibodies	**45**	**44**	**1**	**1**
HBs antigen (Hepatitis B)	10	10	0	0
anti HBs antibodies (Hepatitis B)	10	10	0	0
anti HAV total antibodies (Hepatitis A)	5	5	0	0
anti HAV IgM antibodies (Hepatitis A)	5	5	0	0
anti Treponema pallidum antibodies (Syphilis)	10	10	0	0
anti Dengue antibodies	10	10	0	0
anti Chagas antibodies	10	10	0	0
anti Flu influenzae antibodies	10	10	0	0
Rheumatoid factors	12	12	0	0
anti Mouse antibodies (HAMA)	20	20	0	0
anti nuclear antibodies (ANA)	10	10	0	0
anti smooth muscles antibodies (SMA)	10	10	0	0
Multiparous women	10	10	0	0
Pregnant women	10	10	0	0
Patients with non infectious cirrhosis	4	4	0	0
Myeloma	**21**	**20**	**1**	**1**
Dialysed patients	6	6	0	0
Patients with chronic renal failure	10	10	0	0
total	**354**	**351**	**3**	**2**

9.4. Hook effect

The existence of a possible hook effect was studied by testing 5 specimens with high titers at different dilutions. The equivalence of results observed among non-diluted and diluted specimens indicates the absence of the hook effect.

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Използвайте предпазни ръкавици/предпазно облекло/предпазни очила/предпазна маска за лице. ПРИ КОНТАКТ С ОЧИТЕ: Промивайте внимателно с вода в продължение на няколко минути. Свалете контактните лещи, ако има такива и доколкото това е възможно. Продължавайте да промивате. ПРИ ПОГЛЪЩАНЕ: изплакнете устата. НЕ предизвиквайте повръщане. ПРИ КОНТАКТ С КОЖАТА (или косата): Незабавно свалете цялото замърсено облекло. Облейте кожата с вода/вземете душ При поява на кожно дразнене или обрив на кожата: Потърсете медицински съвет/помощ. Изхвърлете съдържанието/контейнера в съответствие с местните/регионалните/националните/ международните разпоредби.

(CZ)
Nebezpečí
Způsobuje těžké poleptání kůže a poškození očí. Může vyvolat alergickou kožní reakci.
Používejte ochranné rukavice/ochranný oděv/ochranné brýle/obličejový štít. PŘI ZASAŽENÍ OČÍ: Několik minut opatrně vyplachujte vodou. Vyjměte kontaktní čočky, jsou-li nasazeny a pokud je lze vyjmout snadno. Pokračujte ve vyplachování. PŘI POŽITÍ: Vypláchněte ústa. NEVYVOLÁVEJTE zvracení. PŘI STYKU S KŮŽÍ (nebo s vlasy): Veškeré kontaminované části oděvu okamžitě svlékněte. Opláchněte kůži vodou/osprchujte. Při podráždění kůže nebo vyrážce: Vyhledejte lékařskou pomoc/ošetření. Obsah/nádobu likvidujte v souladu s místními/regionálními/národními/mezinárodními předpisy.

(DE)
Gefahr
Verursacht schwere Verätzungen der Haut und schwere Augenschäden. Kann allergische Hautreaktionen verursachen. Schutzhandschuhe/Schutzkleidung/Augenschutz/Gesichtsschutz tragen. BEI KONTAKT MIT DEN AUGEN: Einige Minuten lang behutsam mit Wasser spülen. Vorhandene Kontaktlinsen nach Möglichkeit entfernen. Weiter spülen. BEI VERSCHLUCKEN: Mund ausspülen. KEIN Erbrechen herbeiführen. BEI KONTAKT MIT DER HAUT (oder dem Haar): Alle beschmutzten, getränkten Kleidungsstücke sofort ausziehen. Haut mit Wasser abwaschen/duschen. Bei Hautreizung oder -ausschlag: Ärztlichen Rat einholen/ärztliche Hilfe hinzuziehen. Entsorgung des Inhalts / des Behälters gemäß den örtlichen / regionalen / nationalen/ internationalen Vorschriften.

(DK)
Fare
Forårsager svære forbrændinger af huden og øjenskader. Kan forårsage allergisk hudreaktion.
Bær beskyttelseshandsker/beskyttelsestøj/øjenbeskyttelse/ ansigtsbeskyttelse VED KONTAKT MED ØJNENE: Skyl forsigtigt med vand i flere minutter. Fjern eventuelle kontaktlinser, hvis dette kan gøres let. Fortsæt skylning. I TILFÆLDE AF INDTAGELSE: Skyl munden. Fremkald IKKE opkastning. VED KONTAKT MED HUDEN (eller håret): Tilsmudset tøj tages straks af/fjernes. Skyl/brus huden med vand. Ved hudirritation eller udslet: Søg lægehjælp. Bortskaffelse af indholdet/beholderen i henhold til de lokale/regionale/nationale/internationale forskrifter.

(EE)
Ettevaatust
Põhjustab rasket nahasöövitust ja silmakahjustusi. Võib põhjustada allergilist nahareaktsiooni.
Kanda kaitsekindaid/kaitserõivastust/kaitseprille/kaitsemaski. SILMA SATTUMISE KORRAL: loputada mitme minuti jooksul ettevaatlikult veega. Eemaldada kontaktläätsed, kui neid kasutatakse ja kui neid on kerge eemaldada. Loputada veel kord. ALLANEELAMISE KORRAL: loputada suud. MITTE kutsuda esile oksendamist. NAHALE (või juustele) SATTUMISE KORRAL: võtta viivitamata kõik saastunud rõivad seljast. Loputada nahka veega/loputada duši all. Nahaärrituse või _obe korral: pöörduda arsti poole. Sisu/konteineri käitlus vastavuses kohalike/regionaalsete/rahvuslike/rahvusvaheliste nõuetega.

(EN)
Danger
Causes severe skin burns and eye damage. May cause an allergic skin reaction.
Wear protective gloves/protective clothing/eye protection/face protection. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. IF SWALLOWED: rinse mouth. Do NOT induce vomiting. IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower. If skin irritation or rash occurs: Get medical advice/attention. Dispose of contents/container in accordance with local/regional/national/international regulations.

(ES)
Peligro
Provoca quemaduras graves en la piel y lesiones oculares graves. Puede provocar una reacción alérgica en la piel.
Llevar guantes que aíslen del frío/gafas/máscara. EN CASO DE CONTACTO CON LOS OJOS: Aclarar cuidadosamente con agua durante varios minutos. Quitar las lentes de contacto, si lleva y resulta fácil. Seguir aclarando. EN CASO DE INGESTIÓN: Enjuagarse la boca. NO provocar el vómito. EN CASO DE CONTACTO CON LA PIEL (o el pelo): Quitarse inmediatamente las prendas contaminadas. Aclararse la piel con agua o ducharse. En caso de irritación o erupción cutánea: Consultar a un médico. Eliminar el contenido o el recipiente conforme a la reglamentación local/regional/nacional/ internacional.

(FI)
Vaara
Voimakkaasti ihoa syövyttävää ja silmiä vaurioittavaa. Voi aiheuttaa allergisen ihoreaktion.
Käytä suojakäsineitä/suojavaatetusta/silmiensuojainta/ kasvonsuojainta. JOS KEMIKAALIA JOUTUU SILMIIN: Huuhdo huolellisesti vedellä usean minuutin ajan. Poista piilolinssit, _edical voi tehdä helposti. Jatka huuhtomista. JOS KEMIKAALIA ON NIELTY: Huuhdo suu. EI saa oksennuttaa. JOS KEMIKAALIA JOUTUU IHOLLE (tai hiuksiin): Riisu saastunut vaatetus välittömästi. Huuhdo/suihkuta iho vedellä. Jos ilmenee ihoärsytystä tai ihottumaa: Hakeudu lääkäriin. Säilytä säiliö(t) noudattaen paikallisia/alueellisia/kansallisia/ kansainvälisiä määräyksiä.

(FR)
Danger
Provoque des brûlures de la peau et des lésions oculaires graves. Peut provoquer une allergie cutanée.
Porter des gants de protection/des vêtements de protection/un équipement de protection des yeux/du visage. EN CAS DE CONTACT AVEC LES YEUX: rincer avec précaution à l'eau pendant plusieurs minutes. Enlever les lentilles de contact si la victime en porte et si elles peuvent être facilement enlevées. Continuer à rincer. EN CAS D'INGESTION: rincer la bouche. NE PAS faire vomir. EN CAS DE CONTACT AVEC LA PEAU (ou les cheveux): enlever immédiatement les vêtements contaminés. Rincer la peau à l'eau/se doucher. En cas d'irritation ou d'éruption cutanée: consulter un médecin. Éliminer le contenu/récipient conformément à la réglementation locale/régionale/nationale/internationale.

(GR)
Κίνδυνος
Προκαλεί σοβαρά δερματικά εγκαύματα και οφθαλμικές βλάβες. Μπορεί να προκαλέσει αλλεργική δερματική αντίδραση.
Να φοράτε προστατευτικά γάντια/προστατευτικά ενδύματα/μέσα ατομικής προστασίας για ταμάτια/πρόσωπο. ΣΕ ΠΕΡΙΠΤΩΣΗ ΕΠΑΦΗΣ ΜΕ ΤΑ ΜΑΤΙΑ: Ξεπλύνετε προσεκτικά με νερό για αρκετά λεπτά. Εάν υπάρχουν φακοί επαφής, αφαιρέστε τους, εφόσον είναι εύκολο. Συνεχίστε να ξεπλένετε. ΣΕ ΠΕΡΙΠΤΩΣΗ ΚΑΤΑΠΟΣΗΣ: Ξεπλύνετε το στόμα. ΜΗΝ προκαλέσετε εμετό. ΣΕ ΠΕΡΙΠΤΩΣΗ ΕΠΑΦΗΣ ΜΕ ΤΟ ΔΕΡΜΑ (ή με τα μαλλιά): Αφαιρέστε αμέσως όλα τα μολυσμένα ενδύματα. Ξεπλύνετε το δέρμα με νερό/στο ντους. Εάν παρατηρηθεί ερεθισμός του δέρματος ή εμφανιστεί εξάνθημα: Συμβουλευθείτε/Επισκεφθείτεγιατρό. Απορρίψτε τα περιεχόμενα/δοχείο σύμφωνα με τους τοπικούς/εθνικούς/διεθνείς κανονισμούς.

(HR)
Ppasnost
Uzrokuje teške opekline kože i ozljede oka. Može izazvati alergijsku reakciju na koži.
Nositi zaštitne rukavice/zaštitnu odijelo/zaštitu za oči/zaštitu za lice. U SLUČAJU DODIRA S OČIMA: oprezno ispirati vodom nekoliko minuta. Ukloniti kontaktne leće ukoliko ih nosite i ako se one lako uklanjaju. Nastaviti ispiranje. AKO SE PROGUTA: isprati usta. NE izazivati povraćanje. U SLUČAJU DODIRA S KOŽOM (ili kosom): odmah ukloniti/skinuti svu zaganenu odjeću. Isprati kožu vodom/tuširanjem. U slučaju nadražaja ili osipa na koži: zatražiti savjet/pomoć liječnika. Odložite sadržaje /spremnike u skladu s lokalnim/regionalnim/nacionalni/ medunarodnim odredbama.

(HU)
Veszély
Smarkiai nudegina odą ir pažeidžia akis. Allergiás bőrreakciót válthat ki.
Védőkesztyű/védőruha/szemvédő/arcvédő használata kötelező. SZEMBE KERÜLÉS esetén: Több percig tartó óvatos öblítés vízzel. Adott esetben a kontaktlencsék eltávolítása, ha könnyen megoldható. Az öblítés folytatása. LENYELÉS ESETÉN: a szájat ki kell öblíteni. TILOS hánytatni. HA BŐRRE (vagy hajra) KERÜL: Az összes szennyezett ruhadarabot azonnal el kell távolítani/le kell vetni. A bőrt le kell öblíteni vízzel/zuhanyozás. Bőrirritáció vagy kiütések megjelenése esetén: orvosi ellátást kell kérni. Az edény tartalmát / a tartályt a helyi/regionális/nemzeti/nemzetközi szabályozásoknak megfelelően kell hulladékként elhelyezni.

(IT)
Pericolo
Provoca gravi ustioni cutanee e gravi lesioni oculari. Può provocare una reazione allergica cutanea.
Indossare guanti/indumenti protettivi/Proteggere gli occhi/il viso. IN CASO DI CONTATTO CON GLI OCCHI: sciacquare accuratamente per parecchi minuti. Togliere le eventuali lenti a contatto se è agevole farlo. Continuare a sciacquare. IN CASO DI INGESTIONE: sciacquare la bocca. NON provocare il vomito. IN CASO DI CONTATTO CON LA PELLE (o con i capelli): togliersi di dosso immediatamente tutti gli indumenti contaminati. Sciacquare la pelle/fare una doccia. In caso di irritazione o eruzione della pelle: consultare un medico. Smaltire il prodotto/recipiente in conformità con le disposizioni locali / regionali / nazionali / internazionali.

(LT)
Pavojinga
Smarkiai nudegina odą ir pažeidžia akis. Gali sukelti alerginę odos reakciją.
Mūvėti apsaugines pirštines/dėvėti apsauginius drabužius/ naudoti akių (veido) apsaugos priemones. PATEKUS Į AKIS: Kelias minutes atsargiai plauti vandeniu. Išimti kontaktinius lęšius, jeigu jie yra ir jeigu lengvai galima tai padaryti. Toliau plauti akis. PRARIJUS: išskalauti burną. NESKATINTI vėmimo. PATEKUS ANT ODOS (arba plaukų): Nedelsiant nuvilkti/pašalinti visus užterštus drabužius. Odą nuplauti vandeniu/čiurkšle. Jeigu sudirginama oda arba ją išberia: kreiptis į gydytoją. Turinį/talpą išpilti (išmesti) - šalinti pagal vietines / regionines / nacionalines / tarptautines taisykles.

(NL)
Gevaar
Veroorzaakt ernstige brandwonden en oogletsel. Kan een allergische huidreactie veroorzaken.
Beschermende handschoenen/beschermende kleding/ oogbescherming/gelaatsbescherming dragen. BIJ CONTACT MET DE OGEN: voorzichtig afspoelen met water gedurende een aantal minuten; contactlenzen verwijderen, indien mogelijk; blijven spoelen. NA INSLIKKEN: de mond spoelen — GEEN braken opwekken. BIJ CONTACT MET DE HUID (of het haar): verontreinigde kleding onmiddellijk uittrekken — huid met water afspoelen/afdouchen. Bij huidirritatie of uitslag: een arts raadplegen. De inhoud en de verpakking verwerken volgens de plaatselijke/regionale/nationale/internationale voorschriften.

(NO)
Fare
Forårsaker alvorlige hudforbrenninger og øyeskader. Kan forårsake allergiske hudreaksjoner.
Bruk vernehansker/verneklær/vernebriller/ansiktsskjerm. VED KONTAKT MED ØYNENE: Skyll forsiktig med vann i opptil flere minutter. Fjern evt. kontaktlinser såfremt dette er lett mulig. Fortsett skyllingen. VED SVELGING: Skyll munnen. IKKE fremkall brekninger. VED HUDKONTAKT (eller kontakt med hår): Alle tilsølte klær må fjernes straks. Vask/dusj huden med vann. Ved hudirritasjon eller -utslett: Kontakt / tilkall lege. Innholdet / emballasjen skal avhendes i henhold til de lokale / regionale / nasjonale / internasjonale forskrifter.

(PL)
Niebezpieczeństwo
Powoduje poważne oparzenia skóry oraz uszkodzenia oczu . Może powodować reakcję alergiczną skóry.
Stosować rękawice ochronne/odzież ochronną/ochronę oczu/ochronę twarzy. W PRZYPADKU DOSTANIA SIĘ DO OCZU: Ostrożnie płukać wodą przez kilka minut. Wyjąć soczewki kontaktowe, jeżeli są i można je łatwo usunąć. Nadal płukać. W PRZYPADKU POŁKNIĘCIA: wypłukać usta. NIE wywoływać wymiotów. W PRZYPADKU KONTATKU ZE SKÓRĄ (lub z włosami): Natychmiast usunąć/zdjąć całą zanieczyszczoną odzież. Spłukać skórę pod strumieniem wody/prysznicem. W przypadku wystąpienia podrażnienia skóry lub wysypki: Zasięgnąć porady/zgłosić się pod opiekę lekarza. Zawartość / pojemnik usuwać zgodnie z przepisami miejscowymi / regionalnymi / narodowymi / międzynarodowymi.

(PT)
Perigo
Provoca queimaduras na pele e lesões oculares graves. Pode provocar uma reacção alérgica cutânea.
Usar luvas de protecção/vestuário de protecção/protecção ocular/protecção facial. SE ENTRAR EM CONTACTO COM OS OLHOS: enxaguar cuidadosamente com água durante vários minutos. Se usar lentes de contacto, retire-as, se tal lhe for possível. Continuar a enxaguar. EM CASO DE INGESTÃO: enxaguar a boca. NÃO provocar o vómito. SE ENTRAR EM CONTACTO COM A PELE (ou o cabelo): despir/retirar imediatamente toda a roupa contaminada. Enxaguar a pele com água/tomar um duche. Em caso de irritação ou erupção cutânea: consulte um médico. Eliminar o conteúdo/recipiente de acordo com a legislação local/regional/nacional/ internacional.

(RO)
Pericol
Provoacă arsuri grave ale pielii şi lezarea ochilor. Poate provoca o reacţie alergică a pielii.
Purtaţi mănuşi de protecţie/îmbrăcăminte de protecţie/echipament de protecţie a ochilor/ chipament de protecţie a feţei. ÎN CAZ DE CONTACT CU OCHII: clătiţi cu atenţie cu apă timp de mai multe minute. Scoateţi lentilele de contact, dacă este cazul şi dacă acest lucru se poate face cu uşurinţă. Continuaţi să clătiţi. ÎN CAZ DE ÎNGHIŢIRE: clătiţi gura. NU provocaţi voma. ÎN CAZ DE CONTACT CU PIELEA (sau părul): scoateţi imediat toată îmbrăcămintea contaminată. Clătiţi pielea cu apă/faceţi duş. În caz de iritare a pielii sau de erupţie cutanată: consultaţi medicul. Aruncaţi conţinutul/containerul în acord cu regulamentele locale/regionale/naţionale/internaţionale.

(SE)
Fara
Orsakar allvarliga frätskador på hud och ögon. Kan orsaka allergisk hudreaktion.
Använd skyddshandskar/skyddskläder/ögonskydd/ ansiktsskydd. VID KONTAKT MED ÖGONEN: Skölj försiktigt med vatten i flera minuter. Ta ur eventuella kontaktlinser om det går lätt. Fortsätt att skölja. VID FÖRTÄRING: Skölj munnen. Framkalla INTE kräkning. VID HUDKONTAKT (även håret): Ta omedelbart av alla nedstänkta kläder. Skölj huden med vatten/duscha. Vid hudirritation eller utslag: Sök läkarhjälp. Innehållet / behållaren avfallshanteras enligt lokala / regionala / nationella / internationella föreskrifter.

(SI)
Nevarno
Povzroča hude opekline kože in poškodbe oči. Lahko povzroči alergijski odziv kože.
Nositi zaščitne rokavice/zaščitno obleko/zaščito za oči/zaščito za obraz. PRI STIKU Z OČMI: previdno izpirajte z vodo nekaj minut. Odstranite kontaktne leče, če jih imate in če to lahko storite brez težav. Nadaljujte z izpiranjem. PRI STIKU Z OČMI: previdno izpirajte z vodo nekaj minut. Odstranite kontaktne leče, če jih imate in če to lahko storite brez težav. Nadaljujte z izpiranjem. PRI STIKU S KOŽO (ali lasmi): takoj odstraniti/sleči vsa kontaminirana oblačila. Izprati kožo z vodo/prho. Če nastopi draženje kože ali se pojavi izpuščaj: poiščite zdravniško pomoč/oskrbo. Vsebino/vsebnik odstranite v skladu z lokalnimi/regionalnimi/narodnimi/mednarodnimi predpisi.

(SK)
Nebezpečenstvo
Provoacă arsuri grave ale pielii şi lezarea ochilor. Môže vyvolať alergickú kožnú reakciu.
Noste ochranné rukavice/ochranný odev/ochranné okuliare/ochranu tváre. PO POŽITÍ: vypláchnite ústa. Nevyvolávajte zvracanie. PO POŽITÍ: vypláchnite ústa. Nevyvolávajte zvracanie. PRI KONTAKTE S POKOŽKOU (alebo vlasmi): Odstráňte/vyzlečte všetky kontaminované časti odevu. Pokožku ihneď opláchnite vodou/sprchou. Ak sa prejaví podráždenie pokožky alebo sa vytvoria vyrážky: vyhľadajte lekársku pomoc/starostlivosť. Zneškodnenie obsahu/obalu v súlade s miestnymi/oblastnými/ národnými/medzinárodnými nariadeniami.

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