PLATELIA™ *C. difficile* TOX A&B

Σ 96 REF 72800

Qualitative detection of *Clostridium difficile* toxins A and B in human stool specimen by enzyme immunoassay

IVD

CE

BIO-RAD

1- INTENDED USE

Platelia™ *C. difficile* Tox A&B is an ELISA immunoassay for the qualitative detection of *Clostridium difficile* toxins A and B in human stool specimen.

The test is to be used as an aid in the diagnosis of *C. difficile* disease (CDI) and in conjunction with the clinical patient history.

2- SUMMARY AND EXPLANATION OF THE TEST

C. difficile infection (CDI) is the most commonly diagnosed bacterial cause of infectious hospital-acquired diarrhea [(1)] in developed countries and caused by *C. difficile*. This organism is an anaerobic spore-forming gram positive bacterium that grows in the intestine and causes a spectrum of clinical syndromes: some people have the bacteria and / or their spores in faeces without symptoms. However, most develop diarrhea which, in severe cases, leads to pseudomembranous colitis [(2)] and sometimes death. Disease is caused by the effects of bacterial cytotoxins which cause haemostasis and tissue necrosis, predominantly in the colon [(3)]. Recent treatment with antibiotics is, in most cases, a prerequisite for the development of CDI by disrupting the normal intestinal flora [(4)]. Certain groups of people are particularly at risk of developing CDI. These include the elderly, those who have recently had surgery, and people with serious underlying diseases. Approximately 20% of individuals who are hospitalized acquire *C. difficile* during hospitalization, and more than 30% of these patients develop diarrhea, making *C. difficile* colitis one of the most common hospital acquired infections.

Management of *C. difficile* involves [(5)] treatment of infected patients, as well as infection control measures to prevent and control further spread of infection. The former requires discontinuation of antibiotic treatment where possible, and treatment with specific antibiotics effective against *C. difficile*. Recommended measures to prevent and control *C. difficile* include prudent use of antibiotics, attention to hand hygiene and environmental cleanliness, early detection of cases and isolation of affected patients to prevent direct spread, as well as contamination of the neighbouring environment.

Then most frequently used tool for detection of *C. difficile* infection was the determination of toxins by cell culture and neutralization of toxin that demonstrated good sensitivity and specificity performance. However, cell culture or cytotoxicity assays are tedious, requires specific equipment and time to result can be up to 72 hours. Consequently, many laboratories use EIA assays to screen for *C. difficile* in diarrheic hospitalised patients. Although more convenient, most toxin detection kits to date have demonstrated limited sensitivity and Positive Predictive Value [(6)].

3- PRINCIPLES OF THE PROCEDURE

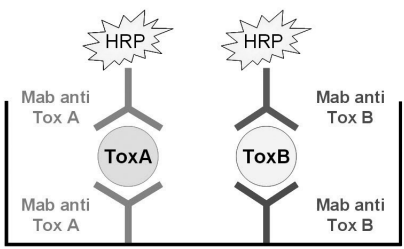
Platelia™ *C. difficile* Tox A&B is a test for the direct detection of *Clostridium difficile* toxins A and B in human stool samples using a one step ELISA immuno-enzymatic method.

The assay uses anti-Toxin A and anti-Toxin B monoclonal antibodies coated on the microplate and labelled with horseradish peroxydase in the conjugate. Samples are prepared by centrifuging liquid, semi-solid or solid stools in Sample Diluent. The supernatant is transferred into the identified microplate well coated with antibodies to *C. difficile* toxins A and B.

Conjugate and sample supernatant are incubated at 37°C for 1 hour in the microwells as well as Calibrator and neat Sample Diluent used as Negative Control. Toxins present in the sample are captured and immobilized between the two specific designed monoclonal antibodies.

After a washing step that removes unbound material, ready-to-use Chromogen substrate is added and incubated at 37°C for 30 minutes to demonstrate the presence of immune-complexes. Reaction is stopped using 1N sulfuric acid solution.

Reading is performed using a spectrophotometer set at 450/620 nm. Presence of a yellow colour indicates presence of the *C. difficile* toxins.



4- REAGENTS

Supplied quantities of reagents have been calculated to allow 96 tests in no more that 6 runs. All reagents are exclusively for *in vitro* diagnostic use.

1. Description

Label		Description	Presentation/ preparation
R1	**Microplate**	**Microplate:** 12 strips with 8 breakable wells, coated with monoclonal antibodies to toxin A and toxin B	1 **Ready-to-use**
R2	**Concentrated Washing Solution (20x)**	**Concentrated Washing Solution (20x):** TRIS-NaCl buffer (pH 7.4), 2% Tween® 20 Preservative : <1.5 % ProClin™ 300	1 x 70 ml **To be diluted**
R5	**Calibrator**	**Calibrator:** TRIS buffer containing *C. difficile* purified toxin A and recombinant toxin B, bovine albumin Serum Preservative : < 1.5% ProClin™ 300	1 x 2.5 ml **Ready-to-use**
R6	**Conjugate (21x)**	**Conjugate (21x):** Monoclonal antibodies to toxins A and B coupled to horseradish peroxydase Preservative : < 1.5% ProClin™ 300	1 x 0.45 ml **To be diluted**
R7	**Diluent**	**Diluent for samples and for Conjugate:** Tris-NaCl buffer, 0.2% Tween® 20, phenol red Preservative : < 1.5% ProClin™ 300	1 x 100 ml **Ready-to-use**
R9	**Chromogen TMB**	**Chromogen:** 3.3'.5.5' tetramethylbenzidine (< 0.1%), H_2O_2 (<1%)	1 x 28 ml **Ready-to-use**
R10	**Stopping Solution**	**Stopping Solution:** 1N sulfuric acid solution	1 x 28 ml **Ready-to-use**
		Plate sealers	4

2. Storage and handling requirements

The kit must be stored at +2-8°C. When the kit is stored at +2-8°C before opening, each component can be used until the expiration date indicated on the outer label of the kit (except specific instructions).

Identification	Conservation
R1	In a closed bag, 8 weeks at +2-8°C (check the presence of desiccant).
R2	Before dilution: until expiry date indicated on the label at 2-30°C in absence of contamination. After dilution: 2 weeks at +2-8°C
R5, R7, R9	After opening, 8 weeks at +2-8°C in absence of contamination.
R6	After opening, 8 weeks at +2-8°C in absence of contamination. After dilution, 8 hours at room temperature (+18-30°C) or up to 24h at +2-8°C
R10	After opening: until expiry date indicated on the label at 2-8°C in absence of contamination

5- WARNINGS AND PRECAUTIONS

For *in vitro* diagnostic use

1. Health and safety instructions

- Wear disposable labcoat, gloves and ocular protection when handling samples and reagents.
- Do not pipette by mouth.
- Do not eat, drink or smoke during the handling of the samples and the test.
- Any material, including washings solutions, that comes directly in contact with samples and reagents containing materials of human origin should be considered capable of transmitting infectious diseases.
- Avoid spilling samples or solutions containing samples. Spills must be rinsed with bleach diluted to 10 %. In the event of a spill with an acid, it must be first neutralized with sodium bicarbonate, and then cleaned with bleach diluted to 10% and dried with adsorbent paper. The material used for cleaning must be discarded in a contaminated residue container.
- Patient samples, reagents containing human origin material, as well as contaminated material and products should be discarded after decontamination only

- either by immersion in bleach at the final concentration of 5 % of sodium hypochlorite during 30 minutes,
- or by autoclaving at 121°C for 2 hours at the minimum.

• Do not introduce solutions containing sodium hypochlorite into the autoclave.

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

For risks and safety recommendations refer to the table at the end of the package insert

2. Precautions related to the procedure

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 within a given run reagents from different lots.

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

NOTE: The washing solution (R2 identified* in green as 20x) may not be mixed with the Washing Solution (R2 identified* in blue as 10x) provided in Bio-Rad reagent kits.

**** on the vial label***

Processing

• Before use, wait for 30 minutes to allow reagents to reach room temperature (+18-30°C).

• Carefully reconstitute or dilute the reagents avoiding any contamination.

• The Positive Control contains biologically active toxin A and should be treated with caution [7].

• Do not carry out the test in the presence of reactive vapors (acid, alkaline, aldehyde vapors) or dust that could alter the enzyme activity of the conjugate.

• **Calibrator (R5) must be thoroughly mixed by pipetting back and forward when distributed**.

- Use glassware thoroughly washed and rinsed with deionized water or, preferably disposable material.
- Washing the microplate is a critical step in the procedure. Follow the recommended number of washings cycles and make sure that all wells are completely filled and then completely emptied. Incorrect washings may lead to inaccurate results.
- Do not allow the microplate to dry between the end of the washings operation and the reagent distribution.
- Never use the same container to distribute the conjugate and the development solution.
- The enzymatic reaction is very sensitive to metal or metal ions. Consequently, do not allow any metal element to come into contact with the various solutions containing the Conjugate or the Chromogen.
- Chromogen solution (R9) should be colourless. The appearance of a blue colour indicates that the reagent cannot be used and must be replaced.
- Use a new pipette tip for each sample.
- Check the pipettes and other equipment for accuracy and correct performance.

6- SPECIMEN

Observe the following recommendations for handling, processing and storage of stool samples:

- Collect all stool samples observing routine precaution into a clean, airtight container with no preservative.
- All stool specimens should be stored at 2°-8°C and tested immediately.
- Ideally, stool specimens should be tested within 24 hours but specimens may be held at 2°-8°C for up to 7 days prior to testing.
- If specimens cannot be tested within 7 days, they should be frozen immediately upon receipt at -20°C or colder.
- A single freeze thaw cycle should not affect results. Repeated freezing and thawing of samples should be avoided.
- Treated supernatant specimens can be stored in a sealed tube for up to 8 hours at 2°-8°C.
- Do not freeze treated samples.
- Do not heat the samples.

7- MATERIAL REQUIRED

1. Materials provided

Refer to section 4, REAGENTS

2. Materials required but not provided

- Vortex mixer.
- Centrifuge for 1.5ml microtubes, speed up to 5,000g
- Microplate reader equipped with 450 nm and 620 nm filters (*).
- Microplate incubator thermostatically set at 37±2°C (*).
- Automatic, semi-automatic or manual microplate washer (*).
- Distilled or deionized water.
- Loops or applicator sticks for solid or formed stools.
- Disposable gloves.
- Goggles or safety glasses.
- Adsorbent paper.
- Automatic or semi-automatic, adjustable or preset, pipettes or multi-pipettes, to measure and dispense 10 µl to 1000 µl, and 1 ml, 2 ml and 10 ml.
- Graduated cylinders of 25 ml, 50 ml, 100 ml and 1000 ml capacity.
- Sodium hypochlorite (bleach) and sodium bicarbonate.
- Container for biohazard waste.
- Disposable tubes.

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

8- INSTRUCTION FOR USE

1. Reagents preparation

- **R1**: Allow 30 minutes at room temperature (+18-30°C) before opening the bag. Take out the carrier tray, return unused strips in the bag immediately and check the presence of desiccant. Carefully reseal the bag and store it at +2-8°C.
- **R2**: Dilute the washing solution (R2) 1/20 in distilled water: for example 50 ml of R2 and 950 ml of distilled water to prepare the ready-to-use washing solution. Prepare 350 ml of diluted washing solution for one plate of 12 strips if washing manually.
- **R6**: Conjugate (R6) is concentrated 21x and must be homogenized before use. Dilute 1/21 in Sample Diluent (R7). For one plate, dilute 300 µl of Conjugate (R6) in 6 ml of Sample Diluent (R7). Divide these volumes by 10 to obtain the volume needed for one strip.

2. Specimen preparation

Stool is the recommended sample type.

If patients' stool samples are liquid or semi-solid, they are prepared by diluting 200µl of liquid stool in 800 µl of Sample Diluent (R7), thoroughly vortexing (15 seconds) and centrifuging in centrifugation tubes of 1.5 ml, at 5,000g during 10 minutes.

If stools are solid, transfer the required stool quantity (equivalent to 200µl) using a loop or applicator stick into 800µl of Sample Diluent and thoroughly vortex (15 seconds) for good extraction before centrifuging.

3. Procedure

Strictly follow the assay procedure and Good Laboratory Practices.

Before use, allow reagents to reach room temperature (+18-30°C).

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

Use all controls with each run to validate the assay results and calculate the cut-off.

1. Carefully establish the distribution and identification plan for controls and patients samples.
2. Prepare the diluted Washing Solution (R2) [*Refer to Section VIII.1*].
3. Take the carrier tray and the strips (R1) out of the protective pouch [*Refer to Section VIII.1*].
4. In individually identified 1.5 ml microtubes, dilute 200 µl of stool in 800 µl of Sample Diluent (R7) and thoroughly vortex (15 seconds). If stools are solid, transfer the required stool quantity (equivalent to 200µl) using a loop or applicator stick and thoroughly vortex (15 seconds) for good extraction. Centrifuge at 5,000g during 10 minutes .
5. Distribute 50µl of diluted Conjugate [*Refer to Section VIII.1*] in each well.
6. Strictly following the indicated sequence below, **immediately** distribute each well with 150µl of Sample Diluent (R7) as Negative Control, Calibrator (R5) in duplicate and supernatant from centrifuged diluted samples [*Refer to Section VIII.2*]. **Calibrator (R5) must be thoroughly mixed by pipetting back and forwards when distributed**.

	1	2	3	4	5	6	7	8	9	10	11	12
A	R7	S6										
B	R5	S7										
C	R5	S8										
D	S1	S9										
E	S2	S10										
F	S3	S11										
G	S4	S12										
H	S5											

7. **Cover the microplate with an adhesive plate sealer**, then press firmly onto the plate to ensure a tight seal. Incubate the microplate **immediately** in a thermostat controlled water bath or in a dry incubator for 1 hour ± 5 minutes at 37°C ± 2°C.
8. At the end of the incubation period, remove the adhesive plate sealer. Aspirate the content of all wells into a container for biohazard waste (containing sodium hypochlorite). Wash the microplate 4 times with 350 µl of the diluted Washing Solution (R2). Invert the microplate and gently tap on adsorbent paper to remove remaining liquid.
9. Quickly distribute into each well and **away from light**, 200 µl of Chromogen solution (R9). **Allow the reaction to develop in the dark for 30 ± 5 minutes at room temperature (+18-30°C).** Do no use adhesive plate sealer during this incubation.
10. Stop the enzymatic reaction by adding 100 µl of Stopping Solution (R10) in each well. Use the same sequence and rate of distribution as for the development solution.
11. Carefully wipe the plate bottom. Read the optical density at 450/620 nm using a plate reader within 30 minutes after stopping the reaction. The strips must always be kept away from light before reading.
12. Before reporting results, check for agreement between the reading and the distribution plan of plate and samples.

9- QUALITY CONTROL

All manufactured reagents are prepared according to our Quality System, starting from reception of raw material to commercialization of the final product. Each lot is submitted to quality control assessments and is released to the market only after conforming to pre-defined acceptance criteria. The records related to production and controls of each single lot are kept within Bio-Rad.

10- INTERPRETATION OF RESULTS

1. Calculation of the Cut-Off value (COV)

COV is calculated as follows: Mean OD (R5)/5.

COV is used for interpretation and calculation of the sample ratio.

Sample ratio (S. Ratio) is the optical density of the sample result (OD. S) compared to the COV: S. Ratio = OD S / COV.

2. Test Validation Criteria

Optical density values and ratio:

$0.600 \leq$ OD R5 ≤ 2.800

(OD1 R5 -OD2 R5)/ mean OD R5 $< 40\%$

R7 Ratio = OD (R7)/COV ≤ 0.60

If validation criteria above are not met, the test run should be repeated.

3. Interpretation of results

The presence or absence of *Clostridium difficile* toxins A and B in the tested sample are determined by comparing optical density of the sample to the cut-off value.

Sample ratio	Result	Interpretation
S. Ratio < 0.90	Negative	A negative result indicates that *C. difficile* toxin A and/or toxin B were absent, degraded or at a concentration too low to be detected in the fecal sample.
0.90 ≤ S. Ratio < 1.10	Equivocal	It is not possible to conclude whether or not C. difficile toxin A and/or toxin B are present in the fecal sample. If a contamination of the patient is suspected, a second sample should be retested.
S. Ratio ≥ 1.10	Positive	A positive test result indicates that *C. difficile* toxin A and/or toxin B are present in the fecal specimen.

A detailed attention must be paid to the other elements of diagnosis for the results close to the gray zone.

11- TEST LIMITATIONS

Diagnosis of *Clostridium difficile* infection can only be established on the basis of a combination of clinical and biological data.

1. The use of Platelia™ *C. difficile* Tox A&B has been validated on human stool samples only.
2. Failure to detect *C. difficile* toxin A and/or toxin B may not preclude *C. difficile* infection but may be due to incorrect sample collection, specimen handling or storage, toxins concentration lower than limit of detection of the assay. In manufacturer conditions of testing, Platelia™ *C. difficile* Tox A&B detected Tox A and Tox B at levels of respectively 1.3 ng/ml and 1.5 ng/ml. It may also be observed due to weakly toxigenic strains, degradation of the toxins or inactivating substances in the fecal specimen.
3. Fecal specimens are complex and show large heterogeneity. It is recommended to test the samples as soon as possible after collection to avoid toxin degradation. However it has been demonstrated that samples could be stored at 2-8°C up to 7 days without significant loss of ratio value. Samples can be stored at -20°C or less for longer periods. Avoid more than 1 freeze-thaw cycle.
4. Platelia™ *C. difficile* Tox A&B has not been validated on paediatric samples.

12- PERFORMANCES CHARACTERISTICS

Performances of Platelia™ *C. difficile* Tox A&B were evaluated on 2 sites on a total of 302 samples.

1. Prevalence

Among the 146 consecutive fresh stool samples from hospitalised patients analyzed by Platelia™ *C. difficile* Tox A&B within the prospective study, 90,4% (132/146) were found negative, 0,7% (1/146) were found doubtful and 8,9% (13/146) were found positive.

2. Relative Sensitivity and Specificity

Performance of Platelia™ *C. difficile* Tox A&B were evaluated on 2 sites on a total of 302 samples. First study was retrospectively tested on a collection of 128 frozen stool samples analyzed in parallel with a competitor EIA and the second was performed prospectively on 174 fresh samples and using cytotoxicity assay as reference method. Results of each study are illustrated below:

Site 1 **Retrospective Study**		**Platelia™ *C. difficile* Tox A&B**			
		Doubtful	**Positive**	**Negative**	**Total**
Reference Competitor EIA	Positive	0	32	0	32
	Negative	0	4	92	96
	Total	0	36	92	128

Performance compared to Competitor EIA	**X/N (%)**	**95% CI**
Relative Sensitivity	32/32 (100%)	89.1% - 100%
Relative Specificity	92/96 (95,8%)	89,7% - 98.9%
Positive Predictive Value	32/36 (88,9%)	73.9% - 96.9%
Negative Predictive Value	92/92 (100%)	96.1% - 100%

Site 1:

Among the four positive samples detected by Platelia™ *C. difficile* Tox A&B but not by Competitor EIA, two were positive using the cytotoxicity assay and could be classified as true positive samples.

Site 2 **Prospective Study**		**Platelia™ *C. difficile* Tox A&B**			**Competitor EIA**		
		Doubtful	**Positive**	**Negative**	**Positive**	**Negative**	**Total**
Reference Cytotoxicity Assay	Positive	2	18	3	15	8	23
	Negative	2	6	143	15	136	151
	Total	4	24	146	30	144	174

Performance compared to cytotoxicity assay	Platelia™ *C. difficile* Tox A&B		Competitor EIA	
	X/N (%)	95% CI	X/N (%)	95% CI
Relative Sensitivity	18/21 (85,7%)*	63.7%-97,0%	15/23 (65,2%)	42,7%-83,6%
Relative Specificity	143/149 (96,0%)*	91,4%-98,5%	136/151 (90,1%)	84,1%-94,3%
Positive Predictive Value	18/24 (75,0%)*	53,3%-90,2%	15/30 (50%)	31,3%-68,7%
Negative Predictive Value	143/146 (97,9%)*	94,1%-99,6%	136/144 (94,4%)	89,3%-97,6%

** Doubtful results excluded from calculation.*

Site 2:

Among the six samples classified as false positive with Platelia™ *C. difficile* Tox A&B, two were also found positive with the Competitor EIA and on the cytotoxicity assay after culture but were not detected with cytotoxicity only test on the stool (true positive). Three were detected as non specific reactions with Platelia™ *C. difficile* Tox A&B.

Among the three samples classified as false negative with Platelia™ *C. difficile* Tox A&B, two were also negative on the Competitor EIA.

3. Cross Reactivity

The specificity of Platelia™ *C. difficile* Tox A&B was tested on bacterial cultures (>10^8 bact/mL) treated as described for stool samples.

No cross reactivity of Platelia™ *C. difficile* Tox A&B was observed with Rotavirus [3], Adenovirus [5], *Aeromonas hydrophila* [1], *Bacillus cereus* [1], *Bacillus subtilis* [1], *Bacteroides fragilis* (1), *Candida albicans* [1], *Clostridium difficile* non-toxinogen [6], *Clostridium haemolyticum* [1], *Clostridium histolyticum* [1], *Clostridium novyi* [1], *Clostridium perfringens* [1], *Clostridium septicum* [1], *Clostridium sporogenes* [1], *Clostridium sordellii* [1], *Clostridium tetani* [1], *Escherichia coli* [1], *Klebsiella pneumoniae* [1], *Peptostreptococcus anaerobius* [1], *Proteus vulgaris* [1], *Pseudomonas aeruginosa* [1], *Salmonella typhimurium* [1], *Shigella flexneri* [1], *Shigella sonnei* [1], *Staphylococcus aureus* [1] *Streptococcus faecalis* [1], *Vibrio parahaemolyticus* [1], *Yersinia enterocolitica* [1].

Even if no cross reactions were observed on Platelia™ *C. difficile* Tox A&B with *Clostridium sordellii*, toxin homology have been described between this species and *C. difficile* that could lead to potential cross reactivity depending on *C. sordelii* strain.

The Platelia™ *C. difficile* Tox A&B test was also evaluated on various toxinogen referenced *C. difficile* strains. The 6 strains (3 A+/B+; 3 A-/B+) were correctly detected by the test.

4. Interfering substance

Results of Platelia™ *C. difficile* Tox A&B testing are not affected by blood (40 % p/v) , barium sulfate (5 % p/v), metronidazole (12,5 mg/ml), bismuth (5 % p/v), mucin (3,5 % p/v), loperamide (5 % p/v), palmitic acid (40 % p/v) or vancomycin (2,5 mg/ml) present in stool specimens.

However, diosmectite (5 % p/v) could induce a change of status for low positive samples.

5. Precision

- Repeatability

In order to evaluate intra-assay repeatability, one negative, one low positive and one positive sample were tested 30 times during the same run. The sample ratio was calculated for each sample. Results: Mean ratio, Standard Deviation (SD) and Coefficient of Variation (%CV) for each of the 3 specimens are listed in the table below:

N=30	Negative sample	Low Positive sample	Positive sample
Mean	0.46	1.18	4.06
SD	0.023	0.039	0.148
%CV	5.0%	3.3%	3.6%

- Reproducibility

In order to evaluate inter-assay reproducibility, one negative, one low positive and one positive sample were tested in duplicate in two runs per day over a 20 day period. The sample ratio was calculated for each sample. Mean of ratio, Standard Deviation (SD) and Coefficient of Variation (%CV) for each of the 3 specimens are listed in the table below:

N=80	Negative sample	Low Positive sample	Positive sample
Mean	0.36	1.43	4.67
SD	0.073	0.179	0.601
%CV	20.5%	12.5%	12.9%

13- BIOGRAPHY REFERENCES

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7. **Donta, S. T., Sullivan T. and Wilkins T.** 1982. Ditferential Effects of *Clostridium difficile* Toxins on Tissue- Cultured Cells. J. Clin. Microb. 1157-1158



(GB) Irritant
(FR) Irritant
(ES) Irritante
(IT) Irritante
(DE) Reizend
(PT) Irritante
(SE) Irriterande
(DK) Lokalirriterende
(GR) Ερεθιστικό
(PL) Produkt drażniący
(LT) Dirginanti
(HU) Irritatív
(EE) Ärritav
(SK) Dráždivý
(CZ) Dráždivý
(RO) Iritant
(BG) Дразнещ
(LV) Kairinošs
(MT) Irritanti
(NL) Irriterend
(SI) Dražilno
(FI) Ärsyttävä

R43:

(GB) • May cause sensitisation by skin contact.
(FR) • Peut entraîner une sensibilisation par contact avec la peau.
(ES) • Posibilidad de sensibilización en contacto con la piel.
(IT) • Può provocare sensibilizzazione per contatto con la pelle.
(DE) • Sensibilisierung durch Hautkontakt möglich.
(PT) • Pode causar sensibilização em contacto com a pele.
(SE) • Kan ge allergi vid hudkontakt.
(DK) • Kan give overfølsomhed ved kontakt med huden.
(GR) • Μπορεί να προκαλέσει ευαισθητοποίηση σε επαφήμε το δέρμα.
(PL) • Może powodować uczulenie w kontakcie ze skórą.
(LT) • Gali sukelti alergiją susilietus su oda.
(HU) • Bőrrel érintkezve túlérzékenységet okozhat (szenzibilizáló hatású lehet).
(EE) • Kokkupuutel nahaga võib põhjustada ülitundlikkust.
(SK) • Môže spôsobiť senzibilizáciu pri kontakte s pokožkou.
(CZ) • Může vyvolat senzibilizaci při styku s kůží.
(RO) • Poate provoca o sensibilizare în contact cu pielea.
(BG) • Възможна е сенсибилизация при контакт с кожата.
(LV) • Saskaroties ar ādu, var izraisīt paaugstinātu jutīgumu.
(MT) • Jista' jikkaġuna sensitizzazzjoni meta jmiss il-ġilda.
(NL) • Kan overgevoeligheid veroorzaken bij contact met de huid.
(SI) • Stik s kožo lahko povzroči preobčutljivost.
(FI) • Ihokosketus voi aiheuttaa herkistymistä.

S24-37-60:

(GB) • Avoid contact with skin. Wear suitable gloves. This material and its container must be disposed of as hazardous waste.
(FR) • Éviter le contact avec la peau. Porter des gants appropriés. Éliminer le produit et son récipient comme un déchet dangereux.
(ES) • Evítese el contacto con la piel. Úsense guantes adecuados. Elimínense el producto y su recipiente como residuos peligrosos.
(IT) • Evitare il contatto con la pelle. Usare guanti adatti. Questo materiale e il suo contenitore devono essere smaltiti come rifiuti pericolosi.
(DE) • Berührung mit der Haut vermeiden. Geeignete Schutzhandschuhe tragen. Dieses Produkt und sein Behälter sind als gefährlicher Abfall zu entsorgen.
(PT) • Evitar o contacto com a pele. Usar luvas adequadas. Este produto e o seu recipiente devem ser eliminados como resíduos perigosos.
(SE) • Undvik kontakt med huden. Använd lämpliga skyddshandskar. Detta material och dess behållare skall tas om hand som farligt avfall.
(DK) • Undgå kontakt med huden. Brug egnede beskyttelseshandsker under arbejdet. Dette materiale og dets beholder skal bortskaffes som farligt affald.
(GR) • Να φοράτε κατάλληλα γάντια. Το υλικό και ο περιέκτης του να θεωρηθούν κατά τη διάθεσή τους επικίνδυνα απόβλητα.
(PL) • Unikać zanieczyszczenia skóry. Nosić odpowiednie rękawice ochronne. Produkt i opakowanie usuwać jako odpad niebezpieczny.
(LT) • Vengti patekimo ant odos. Mūvėti tinkamas pirštines. Šios medžiagos atliekos ir jos pakuotė turi būti šalinamos kaip pavojingos atliekos.
(HU) • A bőrrel való érintkezés kerülendő. Megfelelő védőkesztyűt kell viselni. Az anyagot és/vagy edényzetét veszélyes hulladékként kell ártalmatlanítani.
(EE) • Vältida kokkupuudet nahaga. Kanda sobivaid kaitsekindaid. Kemikaal ja tema pakend kõrvaldada kui ohtlikud jäätmed.
(SK) • Zabráňte kontaktu s pokožkou. Noste vhodné rukavice. Tento materiál a príslušná nádoba musia byť zlikvidované ako nebezpečný odpad. Tento materiál a príslušná nádoba musia byť zlikvidované ako nebezpečný odpad.
(CZ) • Zamezte styku s kůží. Používejte vhodné ochranné rukavice. Tento materiál a jeho obal musí být zneškodněny jako nebezpečný odpad.
(RO) • A se evita contactul cu pielea. A se purta mănuşi corespunzătoare. Acest produs şi ambalajul său se vor depozita ca un deşeu periculos.
(BG) • Да се избягва контакт с кожата. Да се носят подходящи ръкавици. Този материал и неговата опаковка да се третират като опасен отпадък.

(LV) • Nepieļaut nokļūšanu uz ādas. Strādāt aizsargcimdos. Apglabāt šo produktu un tās iepakojumu kā bīstamos atkritumus.

(MT) • Evita l-kuntatt mal-ġilda. Ilbes ingwanti adatt. Dan il-materjal u l-kontenitur tiegħu għandhom jintremew ma'skart perikoluż.

(NL) • Aanraking met de huid vermijden. Draag geschikte handschoenen. Deze stof en de verpakking als gevaarlijk afval afvoeren.

(SI) • Preprečiti stik s kožo. Nositi primerne zaščitne rokavice. Snov/pripravek in embalažo odstraniti kot nevarni odpadek.

(FI) • Varottava kemikaalin joutumista iholle. Käytettävä sopivia suojakäsineitä. Tämä aine ja sen pakkaus on käsiteltävä ongelmajätteenä.

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