Platelia *Aspergillus* Ag

1 plate - Σ 96 REF 62794

SEMI-QUANTITATIVE IMMUNOENZYMATIC SANDWICH MICROPLATE ASSAY FOR THE DETECTION OF *ASPERGILLUS* GALACTOMANNAN ANTIGEN IN ADULT AND PEDIATRIC SERUM SPECIMENS AND BRONCHOALVEOLAR LAVAGE (BAL) FLUID SPECIMENS.

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IFU compliant with Regulation (EU) 2017/746.

Major changes to the previous version are shaded gray. A gray title indicates significant changes in the content of the chapter. Please read carefully.

For the European Union (Regulation 2017/746/EU), the Summary of Safety and Performances of this device is available via EUDAMED public access https://ec.europa.eu/tools/eudamed.

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1. INTENDED USE

The Platelia *Aspergillus* Ag test is a semi-quantitative immunoenzymatic sandwich microplate assay for the detection of *Aspergillus* galactomannan antigen in adult and pediatric serum specimens and bronchoalveolar lavage (BAL) fluid specimens. Platelia *Aspergillus* Ag is a test which, when used in conjunction with other diagnostic procedures, such as microbiological culture, histological examination of biopsy specimens and radiographic evidence, can be used as an aid in the diagnosis of invasive aspergillosis, notably for neutropenic patients or patients treated with immunosuppressants and corticosteroids.
The Platelia *Aspergillus* Ag test can also be used as an aid to monitor antifungal treatment efficacy based on galactomannan index evolution.
The Platelia *Aspergillus* Ag assay can be used manually or on automated microplate systems.

2. SUMMARY AND EXPLANATION OF THE TEST

Aspergillus infections usually start in the lung as the port of entry following inhalation of *Aspergillus* spores which are present in the environment. Invasive forms, which have been increasing for the past 10 years, constitute the most serious infections and a life-threatening disease with very high mortality [1].
Invasive aspergillosis mainly occurs in the respiratory system, but can disseminate to other organs, affecting critically ill patients, including pediatric patients [2–8]: neutropenic patients with malignancies [9–16] or immunocompromised [17], and patients treated with immunosuppressants (solid organ or bone marrow transplantation [18–21] and corticosteroids therapy [22]). Aspergillosis infections are also reported in patients with pulmonary disease [4,23] or infections [24,25], peritoneal dialysis patients [26] and patients receiving parenteral nutrition [27].
Aspergillus is rarely isolated from blood culture, so the diagnosis is often based on non-specific diagnostic or radiological evidence (clinical symptoms, CT scan, chest X-ray, etc.). Unfortunately, these methods lack both sensitivity and specificity, particularly in the early stages of infection, when the diagnosis is often missed. The Bio-Rad Platelia *Aspergillus* Ag detects circulating galactomannan (GM), a major exo-antigen component of the *Aspergillus* cell wall, which is released during their growth. Low levels of the circulating GM antigen are detected in biological fluids so it is the first Clinical Biomarker Qualified by the EORTC/MSG consensus group in 2008 [28]; and it is part of the EORTC-MSG criteria used to define and classify the Invasive Aspergillosis [29]. GM detection in serum and BAL has proven to be useful for the early diagnosis of aspergillosis [17,30]: it is faster than culture methods [31], minimizes the need for invasive specimens [23] and avoids the environmental contamination leading to false positive results [32].
Testing for soluble GM antigen in human serum is the gold standard serological method [29] to aid in the diagnosis of invasive aspergillosis [33–38].
In addition, the detection of GM antigen in BAL has proven to be advantageous for the diagnosis of invasive aspergillosis [39–42], as a non-invasive, less traumatic procedure than lung biopsy [41], in intensive care unit patients [43], hematopoietic stem cell transplantation patients [44,45] and in solid organ transplant recipients [46–51].

3. PRINCIPLES OF THE PROCEDURE

The Platelia *Aspergillus* Ag test is a one-step immunoenzymatic sandwich microplate assay which detects galactomannan (GM) in human serum and BAL fluid. The assay uses the rat monoclonal antibody EBA-2, which is directed against *Aspergillus* GM and has been characterized in previous studies [52–54].
The monoclonal antibodies are used to:

- Coat the wells of the microplate and bind the antigen.
- Detect the antigen bound to the sensitized microplate (conjugate reagent: peroxidase-linked monoclonal antibodies).

Serum or BAL fluid specimens are heat-treated in the presence of EDTA in order to dissociate immune complexes and to precipitate proteins that could possibly interfere with the test [55].

The treated specimens and conjugate are added to the wells coated with monoclonal antibodies and incubated. A monoclonal antibody - GM - monoclonal antibody / peroxidase complex is formed in the presence of GM antigen.

The strips are washed to remove any unbound material. Next, the Chromogen TMB Solution is added, which will react with the complexes bound to the well to form a blue colour reaction.

The enzyme reaction is stopped by the addition of acid, which changes the blue colour to yellow. The absorbance (optical density, OD) of the specimens and controls is determined with a spectrophotometer set at 450 and 620/630 nm wavelengths.

4. REAGENTS

4.1 Description

Identification on label		Description	Presentation/ Preparation 62794
R1	**Microplate**	**Microplate** 12 strips of 8 wells coated with anti-galactomannan rat monoclonal antibodies Specific ID number = 85	1 plate **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**
R3	**Negative Control Serum**	**Negative Control Serum** Human serum negative for HBs antigen, anti-HIV-1, anti-HIV-2 and anti-HCV antibodies Preservative: ProClin 300 - 0.3%	2 vials 1.7 mL **Ready to use**
R4	**Cut-off Control Serum**	**Cut-off Control Serum** Human serum containing galactomannan and negative for HBs antigen, anti-HIV-1, anti-HIV-2 and anti-HCV antibodies Preservative: ProClin 300 - 0.3%	2 vials 1.7 mL **Ready to use**
R5	**Positive Control Serum**	**Positive Control Serum** Human serum containing galactomannan and negative for HBs antigen, anti-HIV-1, anti-HIV-2 and anti-HCV antibodies Preservative: ProClin 300 - 0.3%	2 vials 1.7 mL **Ready to use**
R6	**Conjugate**	**Conjugate** Anti-galactomannan rat monoclonal antibody / peroxidase labelled Preservative: ProClin 300 - 0.3%	1 vial 8 mL **Ready to use**
R7	**Sample Treatment Solution**	**Sample Treatment Solution** EDTA Acid Solution	1 vial 13 mL **Ready to use**
R9	**Chromogen TMB**	**Chromogen TMB Solution** Solution containing < 0.1% 3.3', 5.5' tetramethylbenzidine (TMB) and <1.0% H_2O_2	1 vial 28 mL **Ready to use**
R10	**Stopping Solution**	**Stopping Solution** Sulphuric acid solution (H_2SO_4 1N)	1 vial 28 mL **Ready to use**

4.2 Storage and handling requirements

This kit should be stored at +2-8°C. Open reagents must be stored according to the instructions below.

Identification	Conservation
R1	After opening the vacuum-sealed pouch, store the microwell strips at +2-8°C for up to 8 weeks in their original pouch with desiccant, resealed with tape.
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 until the expiry date, even once opened.
R3, R4, R5, R6, R7, R9	After opening, these reagents stored at +2-8°C are stable for 8 weeks if they are free of contamination.
R10	After this reagent stored at +2-8°C is opened, it is stable until the validity date shown on the label if there is no contamination.

5. WARNING AND PRECAUTIONS

For *in vitro* diagnostic use.
Device for professional users in a laboratory environment only.

For a patient/user/third party in the European Union and in countries with identical regulatory regime (Regulation 2017/746/EU on In vitro Diagnostic Medical Devices); if, during the use of this device or as a result of its use, a serious incident occurs, please report it to the manufacturer and to your national Competent Authority.

5.1 Health and safety precautions

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

The test kit contains human blood components. 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 the 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 (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. The area should be decontaminated with a chemical disinfectant.

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

Dispose of all specimens and materials 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 precautionary statements in this test kit, please refer to the H and P codes on the labels and the information provided at the end of this instruction for use. The Safety Data Sheet is available on www.bio-rad.com.

5.2 Precautions related to the procedure

5.2.1 Preparing

- DO NOT USE the kit if the packaging of any component is damaged.
- DO NOT USE expired reagents.
- **Before use, wait for 30 minutes for the reagents to stabilize at room temperature (+18-30°C).**
- Mix every reagent thoroughly before use.
- Mix the Concentrated Washing Solution (R2) thoroughly before preparing the working Washing Solution, exercising care to avoid microbial contamination.
- Carefully reconstitute the reagents, avoiding any contamination.
- The use of disposable equipment is to be preferred. If using glassware, wash thoroughly and rinse with deionized water.
- Pyrogen-free equipment is optimal, but standard equipment can be used with adequate precautions. Use clean, dust-free equipment (tubes, tips, containers, etc.) to minimize the possibility of contamination with *Aspergillus* spores from the environment. Because GM is heat-stable, sterilization of equipment used does not guarantee the absence of contaminating antigen.
- Limit exposure of solutions (sera, BAL fluid, Sample Treatment Solution, Conjugate) or open containers (plates, tubes, pipettes) to ambient air.
- Do not mix or use reagents from different lots within a test run.
- Do not allow the microplate to dry between the end of the washing operation and reagent dispense.
- The name of the test, as well as a specific identification (ID) number for the test, are written on the frame of each microplate. This specific identification number is stated on each strip too.

  Platelia *Aspergillus* Ag: Specific ID number = 85
- 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.
- Do not mix reagents from other kits that have different lot numbers, with the exception of the Washing Solution (R2, identification*: 20x coloured green), the Chromogen (R9, identification*: TMB coloured turquoise) and the Stopping Solution (R10, identification*: 1N coloured red), provided that these reagents are strictly equivalent and that the same lot number is used within a given test run.

  *REMARK: **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***
- When using a multichannel pipette, transfer the Chromogen TMB solution or the Conjugate solution in a clean plastic reservoir. Single-use plastic reservoirs are recommended. When using reusable plastic reservoirs, they can be cleaned by overnight soaking in distilled water or Washing Solution.
- The Chromogen Solution (R9) must be colourless. The appearance of a blue colour indicates the reagent is contaminated and should not be used.
- 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.
- Never use the same container to dispense the Conjugate and the Chromogen TMB Solution.

5.2.2 Processing

- FROZEN SERUM SPECIMENS STORED IN UNKNOWN CONDITIONS MAY GIVE FALSE POSITIVE RESULTS DUE TO CONTAMINATION WITH FUNGUS AND/OR BACTERIA.
- Adherence to the instructions for use is necessary to ensure proper performance of this product.
- The controls must be heat-treated with the Sample Treatment Solution (R7), like the patient specimens, in order to serve as treatment controls.
- For the treatment of specimens and controls, tubes must be placed in the heating device only when the prescribed temperature can be reached inside the tube: 120°C in a heat block and 100°C in a boiling water bath. Check that the temperature complies with specifications by using a calibrated thermometer fitted into a tube containing mineral oil and placed in the heating device.

- Strict compliance with the prescribed temperature and the prescribed turn-around time, and use of recommended equipment are essential for the success of the test.
- If a heat block is used to treat specimens and controls, the tubes should fit perfectly within the wells to ensure close tube-to-wall contact, allowing maximum heat retention.
- Each run of this assay must proceed to completion without interruption after it has been started. A delay shorter than 5 minutes between two steps is acceptable.
- Check the pipettes and other equipment for accuracy and correct operation.
- Never use the same container to dispense the Conjugate and the Chromogen TMB Solution.
- Do not carry out the test in the presence of reactive vapours (acid, alkaline, aldehyde vapours) or dust that could alter the enzymatic activity of the Conjugate.
- Use a new dispense tip for each specimen.
- Dispense the specimen immediately after the Conjugate dispense.
- Carefully follow the washing procedures described to obtain optimum test performance: respect the recommended number of washing cycles and make sure that all wells are completely filled and then completely emptied. With some instruments, it may be necessary to optimize the washing procedure (increase the number of cycles of washing steps and/or the volume of wash buffer for each cycle) to obtain an acceptable level of OD background for the negative specimens.
- Contact your local commercial representative for adaptations and special procedures.

6. SPECIMENS

This test is performed from native undiluted serum or BAL fluid from adults and pediatric patients.

6.1 Serum

Collect blood specimens according to standard laboratory procedures. Serum specimens must be uncontaminated with fungal spores and/or bacteria. Transport and store specimens in sealed tubes, unexposed to air. Unopened specimens can be stored at +2-8°C for up to 5 days prior to testing. After initial opening, specimens can be stored at +2-8°C for 48 hours prior to testing. For longer storage, store the serum specimens frozen at -20°C for up to 11 months [14].

FROZEN SERUM SPECIMENS STORED IN UNKNOWN CONDITIONS MAY GIVE FALSE POSITIVE RESULTS DUE TO CONTAMINATION WITH FUNGUS AND/OR BACTERIA.

Serum specimens can be subjected to a maximum of 4 freeze/thaw cycles. Previously frozen specimens should be thoroughly mixed after thawing prior to testing.

The results are not affected by specimens containing 20 mg/L bilirubin, lipemic specimens containing 2 g/L triglyceride or hemolyzed specimens containing 500 mg/dL hemoglobin. Interferences related to excess albumin have not been tested.

Do not decomplement sera.

6.2 BAL fluid

Collect BAL fluid specimens according to standard laboratory procedures. BAL fluid specimens must be collected in sterile saline and may be tested on neat specimens (as is) or supernatants from centrifuged specimens (10,000 rpm for 10 minutes) before proceeding to treat the specimen as per Section 7.

BAL fluid specimens must be uncontaminated with fungal spores and/or bacteria. Transport and store specimens in sealed tubes, unexposed to air. After initial opening, specimens can be stored at +2-8°C for up to 24 hours. For longer storage, store the BAL specimens frozen at -20°C for up to 11 months [14].

FROZEN BAL FLUID SPECIMENS STORED IN UNKNOWN CONDITIONS MAY GIVE FALSE POSITIVE RESULTS DUE TO CONTAMINATION WITH FUNGUS AND/OR BACTERIA.

BAL specimens can be subjected to a maximum of 4 freezing/thawing cycles. Previously frozen specimens should be thoroughly mixed after thawing prior to testing.

7. PROCEDURE

7.1 Materials required but not provided

- Sterile distilled or demineralized water to dilute the Concentrated Washing Solution
- Sodium hypochlorite (household bleach) and sodium bicarbonate
- Absorbent paper
- Disposable gloves
- Adhesive film
- Protective goggles
- Disposable tubes
- If multichannel pipettes used: plastic reservoirs
- Automatic or semi-automatic, adjustable or preset pipettes or multichannel pipettes to measure and dispense 50 µL, 100 µL, 300 µL and 1000 µL
- Graduated cylinders of 25 mL, 50 mL, 100 mL and 1000 mL capacity
- Vortex mixer
- 1.5 mL polypropylene microcentrifuge tubes with airtight stoppers able to withstand heating up to 120°C
    - Screw cap tubes: 1.5 mL conical tubes
      OR
    - Snap cap tubes: 1.5 mL EZ micro test tubes
    - Micro-tube cap locks, to prevent caps from opening during temperature and pressure changes
- Laboratory bench centrifuge for 1.5 mL polypropylene tubes capable of centrifuging at 10,000 x g
- Heat block (single-block or two-block models) or boiling water bath at 100°C (*)
- Floating, circular microcentrifuge rack for a 1 L beaker (in case a boiling water bath is used)
- Thermometer fitted into a tube filled with mineral oil, for heating device temperature monitoring
- Automatic (EVOLIS or EVOLIS *Twin PLUS* Bio-Rad systems*) or semi-automatic processor
- Manual microplate washer
- Microplate incubator thermostatically set at 37°C ± 1°C (*)
- Microplate reader equipped with 450 nm and 620/630 nm filters (*)
- Container for biohazardous waste

(*) Consult your Bio-Rad local representative for detailed information about the equipment recommended by our technical department.

7.2 Reagent preparation

7.2.1 Ready to use reagents

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

Reagent 3 (R3): Negative Control, Reagent 4 (R4): Cut-off Control & Reagent 5 (R5): Positive Control
The controls must be heat-treated with the Sample Treatment Solution (R7), like patient specimens, in order to serve as treatment controls.

Reagent 6 (R6): Conjugate, Reagent 7 (R7): Sample Treatment Solution, Reagent 9 (R9): Chromogen TMB, Reagent 10 (R10): Stopping Solution.

7.2.2 Reagents to reconstitute

Reagent 2 (R2): Concentrated Washing Solution (20X)
Prepare the Working Washing Solution by diluting the Concentrated Washing Solution 20 times in distilled water: for one complete 12 strip microplate (excluding dead volume depending on the equipment used) add 50 mL of R2 in 950 mL of distilled water. Use 960 mL of Working Washing Solution. The Working Washing Solution can be stored for 14 days at +2-30°C.
After opening, the Concentrated Washing Solution stored at +2-30°C is stable until the expiry date indicated on the label, if there is no contamination.

7.3 Assay procedure

Strictly follow the procedure and Good Laboratory Practices.

7.3.1 Treatment of the serum/BAL fluid specimens and of the controls

All controls: Negative (R3), Cut-off (R4) and Positive (R5) must be processed at the same time as serum/BAL fluid specimens:

1. Pipette 300 µL of each test serum/BAL fluid and control into individual 1.5 mL polypropylene tubes.
2. Add 100 µL of Sample Treatment Solution (R7) to each tube.
3. Mix the tubes thoroughly by vortexing.
4. Tightly close the tubes to prevent opening during heating.

   Heat block option:
   Measure the temperature inside the tubes with a thermometer fitted into a tube containing mineral oil.
   When 120°C is reached, place the tubes containing specimens and controls into the block.
   Heat the tubes for **6 minutes at 120°C. (*)**

OR

   Water bath option:
   Measure the temperature inside the tubes with a thermometer fitted into a tube containing mineral oil.
   When 100°C is reached, place the tubes containing specimens and controls in the water bath.
   Heat the tubes for **3 minutes at 100°C. (*)**

5. Carefully remove the hot tubes from the heat block or the boiling water bath and place them in a centrifuge.
6. Centrifuge the tubes at 10,000 x g for 10 minutes. The supernatant is used for the detection of the GM antigen.
7. Test the supernatants using the EIA procedure described below. After preparation, the supernatant may be removed and stored at +2-8°C for up to 48 hours prior to testing. If the analysis of the results indicates retesting is required, another aliquot of the specimen must be treated for testing.

(*) Strict compliance with the prescribed temperature and the prescribed turn-around time and use of the recommended equipment are essential for the success of the test. Do not rely on the temperature displayed by the heating device but check that the temperature complies with the specifications by using a calibrated temperature sensor fitted into a tube containing mineral oil: 120°C must be reached inside the tube in a heat block and 100°C in a boiling water bath.

NB: All specimens treated according to this procedure can also be used for the Platelia *Candida* Ag Plus assay, since the specimen treatment procedures are identical for the two tests.

7.3.2 EIA procedure

Strictly follow the procedure and Good Laboratory Practices.

1. **Place the reagents at room temperature (+18-30°C) for at least 30 minutes before use.**
2. Use the controls with each run to validate the results.
3. Prepare the Working Washing Solution.
4. Prepare a dispense plan for the identification of test serum/BAL fluid specimens and controls in the microplate. Use one well for the Negative Control Serum (R3), two wells for the Cut-off Control Serum (R4), and one well for the Positive Control Serum (R5).

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

5. Remove the support frame and the microwell strips (R1) from the protective pouch. Return any strips that will not be used to the pouch with the desiccant and reseal the pouch carefully.
6. Mix the contents of the R6 vial by inverting before use. Add 50 µL of Conjugate (R6) to each well. Next, add 50 µL of treated serum/BAL supernatant to each well, as described above. Do not add serum/BAL fluid specimens to the wells before the Conjugate.
7. **Cover the plate with a plate sealer** or other means to prevent evaporation, ensuring that the entire surface is covered and watertight.
8. Incubate the microplate in a dry microplate incubator for 90 ± 5 minutes at 37°C (± 1°C).
9. Remove the plate sealer. Aspirate the contents of all wells into a waste container (containing sodium hypochlorite). Wash the plate **5 times with a microplate washer** (using 800 µL of Working Washing Solution). After the last wash, invert the microplate and gently tap on absorbent paper to remove any remaining liquid.
10. Rapidly add 200 µL of the Chromogen TMB Solution (R9) to each well, avoiding exposure to bright light.
11. Incubate the microplate in the dark at +18-30°C for 30 ± 5 minutes. **Do not use adhesive film during this incubation step**.
12. Add 100 µL of Stopping Solution (R10) to each well, following the same sequence and rate of dispense as for the Chromogen Solution. Mix well.
13. Thoroughly wipe the bottom of each plate.
14. Read the optical density of each well at 450 nm (reference filter of 620/630 nm). Microplates must be read **within 30 minutes** of adding the Stopping Solution. The strips must always be kept away from light before reading.
15. Check the concordance between the reader printout and the microplate dispense plan before recording the results.

7.4 Quality control

Use Positive (R4 and R5) and Negative (R3) Controls every time the test is performed.

7.5 Test validation criteria

	Validation criteria
R3	The **index (R3 OD / Mean cut-off control OD)** of the Negative Control Serum must be **< 0.40**
R4	The **OD** of each cut-off control serum must be **≥ 0.300 and ≤ 0.800**
R5	The **index (R5 OD / Mean cut-off control OD)** of the Positive Control Serum must be **> 1.50**

Failure of any of the controls to meet the validation criteria described above renders the assay invalid, and patient specimen results should not be reported. The operator may decide to repeat the assay, after reviewing the procedure, or may contact the manufacturer for assistance. If a repeat assay is performed, then a new aliquot of the same specimen should be used in the repeat assay.

- **Example Calculation:**

Specimen	Absorbance (OD)
Negative Control (R3)	0.116
Cut-off Control (R4)	0.513
	0.533
Positive Control (R5)	1.834

- **Calculations**

Mean Cut-off Control Value

To calculate the mean Cut-off Control (R4) OD, add the OD values for each Cut-off Control replicate and divide the result by 2:
(0.513 + 0.533) ÷ 2 = 0.523

Negative Control Index

To calculate the Negative Control Index, divide the Negative Control OD by the mean Cut-off Control OD:
I = 0.116 / 0.523 = 0.22

Positive Control Index

To calculate the Positive Control Index, divide the Positive Control OD by the mean Cut-off Control OD:
I = 1.834 / 0.523 = 3.51

- **Validation criteria**

In the above example:

- Each Cut-off Control OD is ≥ 0.300 and ≤ 0.800, indicating that the Cut-off Control is valid.
- The Negative Control Index is < 0.40, indicating that the Negative Control is valid.
- The Positive Control Index is > 1.50, indicating that the Positive Control is valid.

The test run in this example is considered to be valid since the results meet the validity criteria for each control.

7.6 Calculation/Interpretation of the results

The presence or absence of GM antigen in the test specimen is determined by calculation of an index for each patient specimen. The index (I) is the OD value of the specimen divided by the mean optical density of the wells containing Cut-off Control Serum.

- **Calculation of the mean Cut-off Control OD**

Add the OD of the two wells containing Cut-off Control Serum (R4) and divide the total by 2.

- **Calculation of an index (I) for each test specimen**

Calculate the following ratio for each test specimen:
I = Specimen OD / Mean Cut-off Control OD

- **Interpretation of sera/BAL fluid with an index < 0.50**

Sera/BAL fluid with an index < 0.50 are considered to be negative for GM antigen.

Note: A negative result may indicate that the patient's result is below the detectable level of the assay. Negative results do not rule out the diagnosis of invasive aspergillosis. Repeat testing is recommended if the result is negative, but the disease is suspected.

- **Interpretation of sera/BAL fluid with an index ≥ 0.50**

Sera/BAL fluid with an index ≥ 0.50 are considered to be positive for GM antigen. For all positive patients, it is recommended that a new aliquot of the same specimen (serum/BAL) be tested.

Note 1: An absorbance value of less than 0.000 may indicate a procedural or instrument error which should be evaluated. That result is invalid and the specimen must be re-run.
Regular screening (twice-weekly) of serum specimens from high-risk patients is recommended to increase the sensitivity and early positivity of the test [56].

Note 2: The Platelia *Aspergillus* Ag test is intended to be used as an aid in the diagnosis of invasive aspergillosis. Positive results obtained with the Platelia *Aspergillus* Ag test should be considered in conjunction with other diagnostic procedures, such as microbiological culture, histological examination of biopsy specimens and radiographic evidence.

Example Calculation:

Specimen	Absorbance (OD)
Negative Control (R3)	0.116
Cut-off Control (R4)	0.513
	0.533
Positive Control (R5)	1.834
Patient Specimen #1	0.134
Patient Specimen #2	0.436
Patient Specimen #3	1.196

- **Calculations**

Refer to the Quality Control (Validation criteria) section for an example of calculations to determine the validity of the assay controls.

Mean Cut-off Control Value

To calculate the mean Cut-off Control (R4) OD, add the OD values for each Cut-off Control replicate and divide the result by 2:(0.513 + 0.533) ÷ 2 = 0.523

Patient Specimen #1

To calculate the index of Patient Specimen #1, divide the OD of Patient Specimen #1 by the mean Cut-off. Control OD:

I = 0.134 / 0.523 = 0.26

In this example, Patient Specimen #1 is negative, since the index of 0.26 is < 0.50.

Patient Specimen #2

To calculate the index of Patient Specimen #2, divide the OD of Patient Specimen #2 by the mean Cut-off. Control OD:

I = 0.436 / 0.523 = 0.83

In this example, Patient Specimen #2 is positive, since the index of 0.83 is ≥ 0.50.

Patient Specimen #3

To calculate the index of Patient Specimen #3, divide the OD of Patient Specimen #3 by the mean Cut-off. Control OD:

I = 1.196 / 0.523 = 2.29

In this example, Patient Specimen #3 is positive, since the index of 2.29 is ≥ 0.50.

8. TEST LIMITATIONS

1. A negative test from serum and/or BAL specimens cannot rule out the diagnosis of invasive aspergillosis. Serum specimens from patients at risk for invasive aspergillosis should be tested twice a week [57].
2. Failure to add specimen or reagent as instructed in the procedure could result in a falsely negative test. **Repeat testing of additional specimens should be considered where there is clinical suspicion of invasive aspergillosis or procedural error**.
3. Contamination of negative patient specimen wells by positive control/patient specimen wells is possible if the contents of one well spill over into another well due to rough handling of the microplate or poor pipetting technique while adding reagents.
4. The performance of the Platelia *Aspergillus* Ag test has not been evaluated with neonatal specimens. There is a higher incidence in the number of false-positive GM results reported in the European literature in specimens from neonatal populations [58–61].
5. The Platelia *Aspergillus* Ag test may exhibit reduced detection of galactomannan in patients with chronic granulomatous disease (CGD) and Job's syndrome [62].
6. The Platelia *Aspergillus* Ag test may exhibit false-positive results with serum specimens when digestive enzymes of fungal origin, like Nortase, are used for enzyme substitution therapy in exocrine pancreatic insufficiency in ICU patients [63].
7. The concomitant use of mould-active anti-fungal therapy in some patients with invasive aspergillosis may result in reduced sensitivity with the Platelia *Aspergillus* Ag test [38,64,65].
8. Other genera of fungi such as *Penicillium*, *Alternaria Paecilomyces*, *Geotrichum* and *Histoplasma* have shown reactivity with rat monoclonal antibody EBA-2 used in the assay for the detection of *Aspergillus* GM. Histoplasmosis should be considered in endemic areas [66–69].
9. Cross-reactivity of BAL fluid specimens with *Mycoplasma pneumoniae* or anesthetic drugs/lubricants used to numb the neck/throat area for the aspiration process has not been evaluated.
10. Positive reactions with no clinical signs:

    The following should be considered with regard to early GM antigen detection in serum or BAL fluid before the appearance of clinical and/or radiological signs. Positive test results without clinical signs are regularly observed, and they have been shown to correspond to "true positive" tests in patients for whom Proven or Probable Invasive Aspergillosis diagnosis is established later on [64]. However, in some particular cases, specific factors should be taken into account when interpreting the test:

    a. Positive test results with no clinical signs have been reported, especially in young children [8,61]. Although some of these cases could be related to real circulation of *Aspergillus* antigens, most cases can be considered to be false-positives [70]. Some studies show an increase of the test's accuracy with successive sampling (twice a week), especially for pediatric patients with high risk [4–7].

    b. Galactofuranose has been detected in various foods, particularly cereals, cereal products and cream desserts [71–73]. Unlike human milk, cow's milk formulas frequently contain high concentrations of GM [58]. Dietary factors must therefore be taken into account in the interpretation of the evolution of antigenemia in young children, and more generally in all patients with an altered intestinal barrier [58,72,74,75]. Any case of positive antigenemia not accompanied by clinical signs should be interpreted even more cautiously in this population of patients.

    c. There have been reports of positive GM test results in patients receiving antibiotics, such as ß-lactams, semi-synthetic penicillins (piperacillin/tazobactam), amoxicillin associated with clavulanic acid in parenteral preparation, and ampicillin [76–78]. Patients receiving piperacillin/tazobactam treatment should be carefully monitored, interpreted cautiously and confirmed by other diagnostic methods. Therefore, semi-synthetic ß-lactam treatments should be taken into account when interpreting the test [71,79,80]. Nevertheless, as the Platelia *Aspergillus* Ag test can detect GM antigen well before clinical or radiological signs appear, the occurrence of invasive aspergillosis cannot be ruled out.

d. Positive reactions in the absence of clinical signs may be observed in patients receiving products containing GM, either parenterally or orally (if there is an alteration of the intestinal barrier). The presence of GM in these products can often be explained by the use of a fermentation process based on fungal microorganisms.

   Thus, if there is a suspicious positive result in the absence of other clinical signs, we recommend investigating the products that the patient is taking and notably their production processes and the origin of the raw materials used [81,82].

11. There have been reports of positive reactions for GM in serum and BAL fluid associated with PLASMA-LYTE in several studies [20,27,47,81]. Therefore, any administration of PLASMA-LYTE should be taken into account when interpreting the results of this test.
12. The results of the Platelia *Aspergillus* Ag test in BAL fluid specimens from non-immunocompromised patients should be interpreted with caution [83].
13. Results close to the cut-off index value (0.5) should be interpreted cautiously and should be supported by other clinical, radiological or laboratory evidence of invasive aspergillosis since no gray zone is included in the interpretation of the assay results [84].
14. In addition, results of the Platelia *Aspergillus* Ag test in BAL fluid specimens with an index of 0.5-1.0 have a lower predictive value than the results of BAL specimens with index values > 1.0. Hence results with index values of 0.5-1.0 should be reviewed and supported by other clinical, radiological or laboratory evidence of invasive aspergillosis [39,48,49,85].

9. PERFORMANCE CHARACTERISTICS

9.1 Analytical performance characteristics

9.1.1 Precision measurement

Repeatability and intermediate precision were studied for the Platelia *Aspergillus* Ag assay using a panel constituted of one low negative, one high negative, one low positive, and one high positive specimen. This panel was tested for repeatability in 32 replicates during the same run and for intermediate precision study in duplicates by 2 operators over a period of 20 days with 2 different runs per day.
Means of Index, Standard Deviations (SD) and Coefficients of Variation (CV) for each specimen were calculated.

9.1.1.1 Repeatability

Table 1: Repeatability results

Specimens	N	Mean Index (S/CO)	Repeatability	
			SD	%CV
Low Negative	31*	0.19	0.010	**5.1**
High Negative	32	0.32	0.023	**7.1**
Low positive	32	0.64	0.041	**6.4**
High positive	32	0.94	0.081	**8.6**

**1 outlier excluded from the calculation*

The CVs obtained on the positive specimens are less than or equal to 10%.

9.1.1.2 Intermediate precision

Table 2: Intermediate precision results

Specimens	N	Mean	Repeatability		Between Run		Between Day		Within Laboratory	
		Index S/CO	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low Negative	80	0.21	0.022	**10.6**	0.024	**11.3**	0.006	**3.0**	0.033	**15.8**
High Negative	80	0.34	0.023	**6.8**	0.045	**13.2**	0.037	**10.8**	0.062	**18.4**
Low positive	80	0.61	0.031	**5.1**	0.071	**11.6**	0.038	**6.3**	0.087	**14.2**
High positive	80	0.92	0.098	**10.7**	0.076	**8.3**	0.007	**0.7**	0.124	**13.6**

The CVs obtained on the positive specimens are less than or equal to 15%.

9.1.1.3 Between-site reproducibility

Intra-assay (within run), inter-assay (within lab) and inter-site (between sites) variability for the Platelia *Aspergillus* Ag test were determined in a study using a panel of 6 pooled patient serum specimens (one negative, one low positive, two medium positive, and two high positive) obtained at three (3) clinical trial sites in North America. Each of the 6 panel members was tested in triplicate (x3) on 3 different days on one lot at two sites and in duplicate (x2) on 3 different days on one lot at the third site. One (1) operator performed all precision testing at each site.
The data were analysed according to the guidelines of the Clinical Laboratory Standards Institute (CLSI). The mean index value, standard deviation (SD), percent coefficient of variation (CV%) were estimated and are illustrated in Table 3 below.

Table 3: Between-site reproducibility results

Specimens	N	Mean Index	Within-run (intra-assay)		Within-site (inter-assay)		Between sites		Total precision	
			SD	%CV	SD	%C%	SD	%CV	SD	%CV
Low Negative	24	0.01	0.010	**10.6**	0.030	31.7	0.024	**25.1**	0.028	**29.6**
Low Positive	24	0.74	0.061	**8.3**	0.135	18.2	0.120	**16.2**	0.127	**17.2**
Med Positive1	24	1.11	0.103	**9.2**	0.266	23.9	0.245	**22.0**	0.236	**21.2**
Med Positive-2	24	1.58	0.105	**6.7**	0.284	18.0	0.264	**16.7**	0.242	**15.3**
High Positive-1	24	2.13	0.121	**5.7**	0.425	20.0	0.407	**19.1**	0.364	**17.1**
High Positive-2	24	4.33	0.171	**4.0**	1.133	26.1	1.120	**25.8**	0.945	**21.8**

9.1.1.4 Reproducibility in BAL fluid (repeatability, intermediate precision and reproducibility)

Inter-assay and intra-assay variability for the Platelia *Aspergillus* Ag test were determined in a study using a panel of 4 pooled patient BAL specimens spiked with purified GM (one negative, one high negative, one low positive and one medium positive) at 3 testing sites (two US clinical testing sites and one internal site). Each of the 4 panel members and the controls were tested in duplicate (x2) in 2 runs per day on 5 different days on one lot (total number of results at each site = 120). Two (2) operators performed all precision testing at each site. The data was analysed according to the guidelines of the Clinical Laboratory Standards Institute (CLSI EP5-A2_Evaluation of Precision Performance of quantitative Measurement Methods [86]. The mean index value, standard deviation (SD), percent coefficient of variation (CV%), within-run precision (intra-assay) and within-site (inter-assay) precision and between site precision for each panel member are illustrated in Table 4 below.

Table 4: Combined site results

ID sample	N reps	Mean Index	Within-run (intra-assay)		Within-site (inter-assay)		Between-site (Total)	
			SD	%CV	SD	CV	%SD	%CV
Negative	60	0.29	NA	**NA**	NA	**NA**	NA	**NA**
High Negative	60	0.50	0.10	**20.5%**	0.14	**27.1%**	0.14	**28.2%**
Low positive	60	0.88	0.08	**8.9%**	0.15	**16.7%**	0.15	**16.7%**
Medium Positive	60	1.35	0.07	**5.0%**	0.15	**11.4%**	0.16	**11.6%**
Positive Control	60	3.72	0.27	**7.1%**	0.42	**11.2%**	0.55	**14.8%**
Negative Control	60	0.11	N/A	**N/A**	N/A	**N/A**	N/A	**N/A**

9.2 Analytical specificity

9.2.1 Cross-reactivity study

A study to evaluate the effect of potentially interfering medical conditions unrelated to invasive aspergillosis was performed with one lot of the Platelia *Aspergillus* Ag kit. The following serum specimens were tested for cross-reactivity with the Platelia *Aspergillus* Ag test. A total of 151 sera were tested.

Table 5: Cross-reactivity study results

Pathology	# Specimens Tested	# Positives
Rheumatoid factor	10	0
ANA positive	10	0
IgG hypergammaglobulinemia	10	0
IgM hypergammaglobulinemia	10	0
Cancer*	11	0
Non-viral cirrhosis (primary biliary;alcohol induced; drug induced)	10	0
Multiple transfusions	10	0
Multiparous females	10	0
HAV	10	0
HCV	10	0
Rubella	10	0
CMV	10	0
Syphilis (RPR+)	10	0
Toxoplasmosis	10	0
Mycoplasma	10	0

* One each of bladder, breast (2), colon, endometrial, lung, prostate, renal, and squamous (3).

9.2.2 Hook effect

To challenge if the Platelia *Aspergillus* test demonstrates a “hook effect”, high titre (6400 ng/mL) GM specimens were diluted in GM-negative serum in two-fold serial dilutions from 6400 to 0.78 ng/mL concentrations.
Results demonstrate the absence of hook effect with the Platelia *Aspergillus* Ag test.

9.3 Clinical performance characteristics

The performance characteristics (specificity, sensitivity, Negative and Positive predictive values, likelihood ratio) of the Platelia *Aspergillus* Ag assay, on serum and BAL fluid, were estimated by clinical testing conducted on eight clinical sites in the United States and in Europe.

9.3.1 Serum

Serum testing was conducted on 1,724 serum specimens collected from 172 adult patients and on 1,954 serum specimens collected from 129 pediatric patients (age ≤ 21 years old) at five different sites.
These patients included adults with bone marrow transplant (BMT), leukemia, allogeneic hematopoietic stem cell transplantation (HSCT), acute myeloid leukemia (AML) or myelodysplastic syndrome, and pediatric patients with BMT, leukemia, severely immunocompromised patients undergoing allogeneic HSCT, or being treated for Graft Versus Host Disease after HSCT, or undergoing a second course of therapy to consolidate remitted AML.
These patients were all sequentially drawn in serum specimens for treatment monitoring purpose (average of 13 specimens per patient).
These populations were classified as follows*:

- Patients without signs of invasive aspergillosis (control patients)
- Patients with probable invasive aspergillosis
- Patients with proven invasive aspergillosis

** The Invasive Fungal Infection Cooperative Group (IFICG) of the European Organization for Research and Treatment of Cancer (EORTC) and the Mycosis Study Group (MSG) of the National Institute of Allergy and Infectious Diseases (NIAID) in 2002 defined criteria for the diagnosis of invasive aspergillosis (IA) in patients with hematologic malignancy or hematopoietic stem cell transplant [87].*

9.3.1.1 Specificity

A. Adults

Specificity by adult patient and by specimen

Specificity was estimated based on results obtained at three sites on a total of 143 bone marrow transplant and leukemia adult patients without signs of invasive aspergillosis (control patients) representing 1,262 specimens.

Table 6: Specificity on adult patients

Site	Number of patients	Specificity	95% Confidence Interval	Number of specimens	Specificity	95% Confidence Interval
1	28	78.6% (22/28)	59.1-91.7%	349	98.0% (342/349)	95.9-99.2%
2	77	93.5% (72/77)	85.5-97.9%	560	98.6% (552/560)	97.2-99.4%
3	38	89.5% (34/38)	75.2-97.1%	353	98.9% (349/353)	97.1-99.7%
Combined Sites	**143**	**89.5% (128/143)**	**83.3-94.0%**	**1,262**	**98.5% (1,243/1,262)**	**97.7-99.1%**

B. Pediatrics

Specificity by pediatric patient and by specimen

Specificity was estimated on results obtained on samples from three sites for a total of 108* immunocompromised pediatric patients without signs of invasive aspergillosis (control patients) representing 1,625 specimens. 4 patients with positive GM antigen results coinciding with piperacillin/tazobactam therapy were excluded.

Table 7: Specificity on pediatric patients and by specimen

Site	Number of patients	Specificity	95% Confidence Interval	Number of specimens	Specificity	95% Confidence Interval
1	44	86.4% (38/44)	72.6-94.8%	794	98.9% (785/794)	97.9-99.5%
4	59	86.4% (51/59)	75.5-93.0%	731	97.8% (715/731)	96.5-98.7%
5	5	100% (5/5)	N/A	100	100% (100/100)	96.4-100%
Combined Sites	**108***	**87.0% (94/108)**	**79.2-92.7%**	**1,625****	**98.5% (1,600/1,625)**	**97.7-99.0%**

Note: 4 patients with positive GM antigen results coinciding with piperacillin/tazobactam therapy were excluded.
****Note: 80 specimens from 4 patients with positive GM antigen results coinciding with piperacillin / tazobactam therapy were excluded.***

9.3.1.2 Sensitivity

Adult and pediatric patients

Sensitivity results are estimated only on patient numbers.
At least one positive result per episode was considered.
Sensitivity was estimated on results obtained at three sites on a total of 29 bone marrow transplant (BMT) and leukemia adult patients; and 17 immunocompromised pediatric patients and diagnosed with proven or probable IA.

Table 8: Sensitivity on adults and pediatric patients

Diagnosis	Population	Number of patients	Sensitivity**
Proven aspergillosis	Adults	11	81.8% (9/11)
	Pediatrics	9	44.4% (4/9)
Probable aspergillosis	Adults	18	77.8% (14/18)
	Pediatrics	8	62.5% (5/8)
Combined proven and probable aspergillosis	Adults	29	79.3% (23/29)
	Pediatrics	17*	52.9% (9/17)

** 8 of the 17 pediatric patients gave negative Aspergillus GM antigen results. All of the 8 patients with negative Aspergillus GM antigen results received therapy with multiple antifungal agents. The concomitant use of mould-active anti-fungal therapy in some patients with IA may result in reduced sensitivity* [64,65].
*** 95% Confidence interval was not calculated for N<30.*

9.3.1.3 Predictive values

Positive and negative predictive values were analysed for the patient population in this study. Based on the actual average of a 16.9% prevalence rate in adults and a 13.6% prevalence rate in pediatric patient observed in this study, positive and negative predictive values were estimated as indicated in the following table.

Table 9: Predictive values on adult and pediatric patients

	Prevalence	PPV	CI 95%	NPV	CI 95%
Adults	16.9%	60.5%	40.9-78.3	95.5%	90.5-97.9
	5%	27.2%	13.7-46.7	98.8%	95.4-99.7
Pediatrics	13.6%	39.1%	22.2-59.2	92.2%	85.3-96.0
	5%	17.6%	6.5-39.8	97.2%	92.1-99.1

The expected prevalence of invasive aspergillosis varies with the patient population. Rates from 5-20% have been reported [22,55]. For patient populations on the lower end of the published prevalence, the positive and negative predictive values were re-calculated using a 5% prevalence rate.

9.3.2 BAL fluid specimens

The sensitivity and specificity of the Platelia *Aspergillus* Ag test with BAL fluid specimens were prospectively evaluated in two studies in the United States on a total of 449 BAL samples from 178 patients (116 BAL specimens from 62 SOT recipients and 333 specimens from 116 lung transplant recipients) and in one retrospective study in Europe on 99 specimens from 99 high-risk hematology patients with and without invasive aspergillosis (according to the EORTC/MSG criteria [28]).
SOT recipient types were heart, kidney, liver and lung.

9.3.2.1 Specificity

Specificity was evaluated on the control patients' population (without invasive aspergillosis): SOT patients without IA and patients with hematological disorders; and according to the presence or absence of mould colonization:

Table 10: Specificity results

Population	Diagnosis	Patients / Specimens	N	N Negative	Specificity %	95% CI
SOT Patients	Controls without colonization	patients	119	108	**90.7%**	84.1 – 95.3%
		specimens	341	330	**96.8%**	94.3 - 98.4%
	Controls with colonization	patients	48	38	**79.2%**	65.0 – 89.5%
		specimens	62	50	**80.6%**	68.6 - 89.6%
	Control Total	patients	167	146	**87.4%**	81.4 – 92.0%
		specimens	403	380	**94.3%**	91.6 - 96.4%
Patients with hematological disorders	Controls without sign of IA	patients/specimens	41	33	**80.5%**	65.1 – 91.2%

9.3.2.2 Sensitivity

Sensitivity was evaluated in solid organ transplant and lung transplant recipients diagnosed with IA as well as hematologic disease patients diagnosed with IA according to the EORTC/MSG criteria [88]. Results are presented in Table 11.

Table 11: Sensitivity results

Population	Diagnosis	Patients/Specimens	N	N positive	%	95% CI
SOT Patients	Probable IA	patients	7	6	**85.7%**	NA*
		specimens	26	13	**50.0%**	NA
	Proven IA	patients	4	3	**75.0%**	NA
		specimens	20	6	**30.0%**	NA
	Total	patients	11	9	**81.8%**	NA
		specimens	46	19	**41.3%**	**27.0 – 56.8%**
Patients with hematological disorders	Probable IA	patients/specimens	27	26	**96.3%**	81.0 – 99.9%
	Proven IA	patients/specimens	31	31	**100%**	88.8 – 100.0%
	Total	patients/specimens	58	57	**98.3%**	90.8 – 100.0%

10. BIBLIOGRAPHY REFERENCES

1. **WHO fungal priority pathogens list to guide research, development and public health action**. Geneva: World Health Organization. Licence: CC BY-NC-SA 3.0 IGO; 2022.
2. Stynen D, Goris A, Sarfati J, Latgé JP: **A new sensitive sandwich enzyme-linked immunosorbent assay to detect galactofuran in patients with invasive aspergillosis**. *J Clin Microbiol* 1995, **33**:497–500.
3. Desai R, Ross LA, Hoffman JA: **The role of bronchoalveolar lavage galactomannan in the diagnosis of pediatric invasive aspergillosis**. *Pediatr Infect Dis J* 2009, **28**:283–286.
4. Agarwal R, Aggarwal AN, Sehgal IS, Dhooria S, Behera D, Chakrabarti A: **Performance of serum galactomannan in patients with allergic bronchopulmonary aspergillosis**. *Mycoses* 2015, **58**:408–412.
5. Çağlar İ, Özkerim D, Tahta N, Düzgöl M, Bayram N, Demirağ B, Hilkay Karapınar T, Sorguç Y, Gözmen S, Dursun V, et al.: **262. Assessment of Serum Galactomannan Test Results of Pediatric Patients with Hematologic Malignancies According to Different Threshold Levels and Consecutive Positivity in Terms of Invasive Aspergillosis Diagnosis: Cross-Sectional Research in a Tertiary Care Hospital**. *Open Forum Infect Dis* 2019, **6**:S145–S146.
6. Couchepin J, Brunel A, Jaton K, Meylan P, Bochud P, Lamoth F: **Role of bi-weekly serum galactomannan screening for the diagnosis of invasive aspergillosis in haematological cancer patients**. *Mycoses* 2018, **61**:350–354.
7. Okuturlar Y, Ozkalemkas F, Ener B, Serin SO, Kazak E, Ozcelik T, Ozkocaman V, Ozkan HA, Akalin H, Gunaldi M, et al.: **Serum galactomannan levels in the diagnosis of invasive aspergillosis**. *Korean J Intern Med* 2015, **30**:899–905.
8. Warris A, Lehrnbecher T, Roilides E, Castagnola E, Brüggemann RJM, Groll AH: **ESCMID-ECMM guideline: diagnosis and management of invasive aspergillosis in neonates and children**. *Clinical Microbiology and Infection* 2019, **25**:1096–1113.
9. Dichtl K, Seybold U, Ormanns S, Horns H, Wagener J: **Comparison of a novel galactomannoprotein ELISA and the Platelia galactomannan ELISA for the diagnosis of invasive aspergillosis**. *Mycoses* 2019, **62**:15.
10. Wang X, Guo G, Cai R, He P, Zhang M: **Utility of serum galactomannan antigen testing combined with chest computed tomography for early diagnosis of invasive pulmonary aspergillosis in patients with hematological malignancies with febrile neutropenia after antifungal drug treatment**. *J Int Med Res* 2019, **47**:783–790.

11. Mikulska M, Furfaro E, De Carolis E, Drago E, Pulzato I, Borghesi ML, Zappulo E, Raiola AM, Grazia CD, Del Bono V, et al.: **Use of Aspergillus fumigatus real-time PCR in bronchoalveolar lavage samples (BAL) for diagnosis of invasive aspergillosis, including azole-resistant cases, in high risk haematology patients: the need for a combined use with galactomannan**. *Medical Mycology* 2019, **57**:987–996.

12. Badiee P, Hashemizadeh Z, Ramzi M, Karimi M, Mohammadi R: **Non-Invasive Methods to Diagnose Fungal Infections in Pediatric Patients with Hematologic Disorders**. *Jundishapur J Microbiol* 2016, **9**.

13. Bellanger AP, Millon L, Berceanu A, Grenouillet F, Grenouillet FE, Larosa F, Deconinck E: **Combining *Aspergillus* mitochondrial and ribosomal QPCR, in addition to galactomannan assay, for early diagnosis of invasive aspergillosis in hematology patients**. *Med Myco* 2015, **53**:760–764.

14. Wheat LJ, Nguyen MH, Alexander BD, Denning D, Caliendo AM, Lyon GM, Baden LR, Marty FM, Clancy C, Kirsch E, et al.: **Long-Term Stability at −20°C of Aspergillus Galactomannan in Serum and Bronchoalveolar Lavage Specimens**. *J Clin Microbiol* 2014, **52**:2108–2111.

15. Da Silva TVM, Carneiro LC, Dos Santos Ramos F, Baethgen LF, Paz AA, Larentis DZ, Daudt LE, Tusset C, Lopes-Bezerra LM, Pasqualotto AC: **PCR as a Screening Test for Invasive Aspergillosis in Haematological Patients: A Pilot Study**. *Mycopathologia* 2014, **177**:111–114.

16. Taremi M, Kleinberg ME, Wang EW, Gilliam BL, Ryscavage PA: **Galactomannan antigen detection using bronchial wash and bronchoalveolar lavage in patients with hematologic malignancies**. *Ann Clin Microbiol Antimicrob* 2015, **14**:50.

17. Zheng J, Gui X, Cao Q, Yang R, Yan Y, Deng L, Lio J: **A Clinical Study of Acquired Immunodeficiency Syndrome Associated Penicillium Marneffei Infection from a Non-Endemic Area in China**. *PLoS ONE* 2015, **10**:e0130376.

18. Singh N, Paterson DL: ***Aspergillus* Infections in Transplant Recipients**. *Clin Microbiol Rev* 2005, **18**:44–69.

19. Barnes PD, Marr KA: **Risks, diagnosis and outcomes of invasive fungal infections in haematopoietic stem cell transplant recipients**. *Br J Haematol* 2007, **139**:519–531.

20. Weinbergerova B, Kocmanova I, Racil Z, Mayer J: **Serological Approaches**. In *Human Fungal Pathogen Identification*. Edited by Lion T. Springer New York; 2017:209–221.

21. Gefen A, Zaidman I, Shachor-Meyouhas Y, Avidor I, Hakim F, Weyl Ben-Arush M, Kassis I: **Serum Galactomannan Screening for Diagnosis of Invasive Pulmonary Aspergillosis in Children After Stem Cell Transplantation or with High-Risk Leukemia**. *Pediatric Hematology and Oncology* 2015, **32**:146–152.

22. Denning DW: **Invasive aspergillosis**. *Clin Infect Dis* 1998, **26**:781–803; quiz 804–805.

23. Ramanan P, Wengenack NL, Theel ES: **Laboratory Diagnostics for Fungal Infections**. *Clinics in Chest Medicine* 2017, **38**:535–554.

24. Badiee P, Amirghofran AA, Ghazi Nour M: **Evaluation of noninvasive methods for the diagnosis of fungal endocarditis**. *Medical Mycology* 2014, **52**:530–536.

25. de Azevedo PZ, Sylvestre TF, Cavalcante R de S, de Carvalho LR, Moris DV, de Oliveira MLCS, Mendes RP: **Evaluation of the Double Agar Gel Immunodiffusion Test and of the Enzyme-Linked Immunosorbent Assay in the Diagnosis and Follow-Up of Patients with Chronic Pulmonary Aspergillosis**. *PLoS One* 2015, **10**:e0134841.

26. Leelahavanichkul A, Pongpirul K, Thongbor N, Worasilchai N, Petphuak K, Thongsawang B, Towannang P, Lorvinitnun P, Sukhontasing K, Katavetin P, et al.: **(1→3)-β–d-Glucan and Galactomannan for Differentiating Chemical "Black Particles" and Fungal Particles Inside Peritoneal Dialysis Tubing**. *Perit Dial Int* 2016, **36**:402–409.

27. Knoth H, Maywald D, Walter W: **In-vitro detection of mannan and galactomannan in components of total parenteral nutrition (TPN)**. *Pharmazie* 2016, doi:10.1691/ph.2016.5797.

28. De Pauw B, Walsh TJ, Donnelly JP, Stevens DA, Edwards JE, Calandra T, Pappas PG, Maertens J, Lortholary O, Kauffman CA, et al.: **Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group**. *Clin Infect Dis* 2008, **46**:1813–1821.

29. Maertens J, Verhaegen J, Lagrou K, Van Eldere J, Boogaerts M: **Screening for circulating galactomannan as a noninvasive diagnostic tool for invasive aspergillosis in prolonged neutropenic patients and stem cell transplantation recipients: a prospective validation**. *Blood* 2001, **97**:1604–1610.

30. Yoshimura K, Suzuki Y, Inoue Y, Nishimoto K, Mori K, Karayama M, Hozumi H, Furuhashi K, Enomoto N, Fujisawa T, et al.: **Utility of serum Aspergillus-galactomannan antigen to evaluate the risk of severe acute exacerbation in chronic obstructive pulmonary disease**. *PLoS ONE* 2018, **13**:e0198479.

31. Moura S, Cerqueira L, Almeida A: **Invasive pulmonary aspergillosis: current diagnostic methodologies and a new molecular approach**. *Eur J Clin Microbiol Infect Dis* 2018, **37**:1393–1403.

32. Cabana ÂL, Mendes JF, Klafke GB, Brandolt TM, Melo AM, Meireles MCA, Xavier MO: **Can Aspergillus fumigatus conidia cause false-positive results in the galactomannan enzyme immunoassay test?** *Rev Soc Bras Med Trop* 2018, **51**:387–389.

33. De Repentigny L, Kaufman L, Cole GT, Kruse D, Latgé JP, Matthews RC: **Immunodiagnosis of invasive fungal infections**. *J Med Vet Mycol* 1994, **32 Suppl 1**:239–252.

34. Erjavec Z, Verweij PE: **Recent progress in the diagnosis of fungal infections in the immunocompromised host**. *Drug Resistance Updates* 2002, **5**:3–10.

35. Latgé JP: **Tools and trends in the detection of Aspergillus fumigatus**. *Curr Top Med Mycol* 1995, **6**:245–281.

36. Verweij PE, Meis JFGM: **Microbiological diagnosis of invasive fungal infections in transplant recipients: Diagnosis of invasive fungal infections**. *Transplant Infectious Disease* 2000, **2**:80–87.

37. Yeo SF, Wong B: **Current Status of Nonculture Methods for Diagnosis of Invasive Fungal Infections**. *Clin Microbiol Rev* 2002, **15**:465–484.

38. Prattes J, Heldt S, Eigl S, Hoenigl M: **Point of Care Testing for the Diagnosis of Fungal Infections: Are We There Yet?** *Curr Fungal Infect Rep* 2016, **10**:43–50.

39. Maertens J, Maertens V, Theunissen K, Meersseman W, Meersseman P, Meers S, Verbeken E, Verhoef G, Van Eldere J, Lagrou K: **Bronchoalveolar Lavage Fluid Galactomannan for the Diagnosis of Invasive Pulmonary Aspergillosis in Patients with Hematologic Diseases**. *CLIN INFECT DIS* 2009, **49**:1688–1693.

40. Salonen J, Lehtonen OP, Teräsjärvi MR, Nikoskelainen J: **Aspergillus antigen in serum, urine and bronchoalveolar lavage specimens of neutropenic patients in relation to clinical outcome**. *Scand J Infect Dis* 2000, **32**:485–490.

41. Sanguinetti M, Posteraro B, Pagano L, Pagliari G, Fianchi L, Mele L, La Sorda M, Franco A, Fadda G: **Comparison of real-time PCR, conventional PCR, and galactomannan antigen detection by enzyme-linked immunosorbent assay using bronchoalveolar lavage fluid samples from hematology patients for diagnosis of invasive pulmonary aspergillosis**. *J Clin Microbiol* 2003, **41**:3922–3925.

42. Verweij PE, Latgé JP, Rijs AJ, Melchers WJ, De Pauw BE, Hoogkamp-Korstanje JA, Meis JF: **Comparison of antigen detection and PCR assay using bronchoalveolar lavage fluid for diagnosing invasive pulmonary aspergillosis in patients receiving treatment for hematological malignancies**. *J Clin Microbiol* 1995, **33**:3150–3153.

43. Meersseman W, Lagrou K, Maertens J, Wilmer A, Hermans G, Vanderschueren S, Spriet I, Verbeken E, Van Wijngaerden E: **Galactomannan in Bronchoalveolar Lavage Fluid: A Tool for Diagnosing Aspergillosis in Intensive Care Unit Patients**. *Am J Respir Crit Care Med* 2008, **177**:27–34.

44. Musher B, Fredricks D, Leisenring W, Balajee SA, Smith C, Marr KA: **Aspergillus galactomannan enzyme immunoassay and quantitative PCR for diagnosis of invasive aspergillosis with bronchoalveolar lavage fluid**. *J Clin Microbiol* 2004, **42**:5517–5522.

45. Sulahian A, Boutboul F, Ribaud P, Leblanc T, Lacroix C, Derouin F: **Value of antigen detection using an enzyme immunoassay in the diagnosis and prediction of invasive aspergillosis in two adult and pediatric hematology units during a 4-year prospective study**. *Cancer* 2001, **91**:311–318.

46. Becker MJ, Lugtenburg EJ, Cornelissen JJ, Van Der Schee C, Hoogsteden HC, De Marie S: **Galactomannan detection in computerized tomography-based broncho-alveolar lavage fluid and serum in haematological patients at risk for invasive pulmonary aspergillosis**. *Br J Haematol* 2003, **121**:448–457.

47. Kwak EJ, Nguyen MH: **Galactomannan detection in bronchoalveolar lavage fluid**. *Curr Fungal Infect Rep* 2008, **2**:206–213.

48. Clancy CJ, Jaber RA, Leather HL, Wingard JR, Staley B, Wheat LJ, Cline CL, Rand KH, Schain D, Baz M, et al.: **Bronchoalveolar Lavage Galactomannan in Diagnosis of Invasive Pulmonary Aspergillosis among Solid-Organ Transplant Recipients**. *J Clin Microbiol* 2007, **45**:1759–1765.

49. Lahmer T, Neuenhahn M, Held J, Rasch S, Schmid RM, Huber W: **Comparison of 1,3-β-d-glucan with galactomannan in serum and bronchoalveolar fluid for the detection of Aspergillus species in immunosuppressed mechanical ventilated critically ill patients**. *Journal of Critical Care* 2016, **36**:259–264.

50. Husain S, Clancy CJ, Nguyen MH, Swartzentruber S, Leather H, LeMonte AM, Durkin MM, Knox KS, Hage CA, Bentsen C, et al.: **Performance Characteristics of the Platelia *Aspergillus* Enzyme Immunoassay for Detection of *Aspergillus* Galactomannan Antigen in Bronchoalveolar Lavage Fluid**. *Clin Vaccine Immunol* 2008, **15**:1760–1763.

51. Paterson DL, Singh N: **Invasive aspergillosis in transplant recipients**. *Medicine (Baltimore)* 1999, **78**:123–138.

52. Latgé JP, Kobayashi H, Debeaupuis JP, Diaquin M, Sarfati J, Wieruszeski JM, Parra E, Bouchara JP, Fournet B: **Chemical and immunological characterization of the extracellular galactomannan of Aspergillus fumigatus.** *Infect Immun* 1994, **62**:5424–5433.

53. Stynen D, Sarfati J, Goris A, Prévost MC, Lesourd M, Kamphuis H, Darras V, Latgé JP: **Rat monoclonal antibodies against Aspergillus galactomannan**. *Infect Immun* 1992, **60**:2237–2245.

54. Wheat LJ, Walsh TJ: **Diagnosis of invasive aspergillosis by galactomannan antigenemia detection using an enzyme immunoassay**. *Eur J Clin Microbiol Infect Dis* 2008, **27**:245–251.

55. Latgé J-P: **Aspergillus fumigatus and Aspergillosis**. *Clin Microbiol Rev* 1999, **12**:310–350.

56. Maertens JA, Klont R, Masson C, Theunissen K, Meersseman W, Lagrou K, Heinen C, Crepin B, Eldere JV, Tabouret M, et al.: **Optimization of the Cutoff Value for the Aspergillus Double-Sandwich Enzyme Immunoassay**. *Clinical Infectious Diseases* 2007, **44**:1329–1336.

57. Verweij PE, Stynen D, Rijs AJ, De Pauw BE, Hoogkamp-Korstanje JA, Meis JF: **Sandwich enzyme-linked immunosorbent assay compared with Pastorex latex agglutination test for diagnosing invasive aspergillosis in immunocompromised patients**. *J Clin Microbiol* 1995, **33**:1912–1914.

58. Gangneux J-P, Lavarde D, Bretagne S, Guiguen C, Gandemer V: **Transient aspergillus antigenaemia: think of milk**. *Lancet* 2002, **359**:1251.

59. Herbrecht R, Letscher-Bru V, Oprea C, Lioure B, Waller J, Campos F, Villard O, Liu K-L, Natarajan-Amé S, Lutz P, et al.: **Aspergillus Galactomannan Detection in the Diagnosis of Invasive Aspergillosis in Cancer Patients**. *JCO* 2002, **20**:1898–1906.

60. Mennink-Kersten MASH, Ruegebrink D, Klont RR, Warris A, Gavini F, Op Den Camp HJM, Verweij PE: **Bifidobacterial Lipoglycan as a New Cause for False-Positive Platelia *Aspergillus* Enzyme-Linked Immunosorbent Assay Reactivity**. *J Clin Microbiol* 2005, **43**:3925–3931.

61. Siemann M, Koch-Dörfler M, Gaude M: **False-positive results in premature infants with the Platelia® *Aspergillus* sandwich enzyme-linked immunosorbent assay**. *Mycoses* 1998, **41**:373–377.

62. Verweij PE, Weemaes CM, Curfs JHAJ, Bretagne S, Meis JFGM: **Failure To Detect Circulating *Aspergillus* Markers in a Patient with Chronic Granulomatous Disease and Invasive Aspergillosis**. *J Clin Microbiol* 2000, **38**:3900–3901.

63. Schroeder I, Dichtl K, Liebchen U, Wagener J, Irlbeck M, Zoller M, Scharf C: **Digestive enzymes of fungal origin as a relevant cause of false positive Aspergillus antigen testing in intensive care unit patients**. *Infection* 2021, **49**:241–248.

64. De Heer K, Gerritsen MG, Visser CE, Leeflang MM: **Galactomannan detection in broncho-alveolar lavage fluid for invasive aspergillosis in immunocompromised patients**. *Cochrane Database of Systematic Reviews* 2019, **2020**.

65. Marr KA, Laverdiere M, Gugel A, Leisenring W: **Antifungal Therapy Decreases Sensitivity of theAspergillus Galactomannan Enzyme Immunoassay**. *Clinical Infectious Diseases* 2005, **40**:1762–1769.

66. Knox KS, Rose AS, Hage CA: **Rapid Fungal Diagnosis: The Utility of Bronchoalveolar Lavage for Pneumocystis and Endemic Mycoses**. *Current Fungal Infection Reports* 2007,

67. Narreddy S, Chandrasekar PH: **False-positive Aspergillus galactomannan (GM) assay in histoplasmosis**. *Journal of Infection* 2008, **56**:80–81.

68. Swanink CM, Meis JF, Rijs AJ, Donnelly JP, Verweij PE: **Specificity of a sandwich enzyme-linked immunosorbent assay for detecting Aspergillus galactomannan**. *J Clin Microbiol* 1997, **35**:257–260.

69. Wheat LJ, Hackett E, Durkin M, Connolly P, Petraitiene R, Walsh TJ, Knox K, Hage C: **Histoplasmosis-Associated Cross-Reactivity in the BioRad Platelia *Aspergillus* Enzyme Immunoassay**. *Clin Vaccine Immunol* 2007, **14**:638–640.

70. Chambon-Pautas C, Costa J-M, Chaumette M-T, Cordonnier C, Bretagne S: **Galactomannan and Polymerase Chain Reaction for the Diagnosis of Primary Digestive Aspergillosis in a Patient with Acute Myeloid Leukaemia**. *Journal of Infection* 2001, **43**:213–214.

71. Ansorg R, van den Boom R, Rath PM: **Detection of Aspergillus galactomannan antigen in foods and antibiotics**. *Mycoses* 1997, **40**:353–357.

72. Letscher-Bru V, Cavalier A, Pernot-Marino E, Koenig H, Eyer D, Waller J, Candolfi E: **Recherche d'antigene galactomannane Aspergillaire circulant par Platelia® Aspergillus: Antigenemies positives persistantes en l'absence d'infection**. *J Mycol Med* 1998, **8**:112–113.

73. Maertens J, Verhaegen J, Demuynck H, Brock P, Verhoef G, Vandenberghe P, Van Eldere J, Verbist L, Boogaerts M: **Autopsy-Controlled Prospective Evaluation of Serial Screening for Circulating Galactomannan by a Sandwich Enzyme-Linked Immunosorbent Assay for Hematological Patients at Risk for Invasive Aspergillosis**. *J Clin Microbiol* 1999, **37**:3223–3228.

74. Verdaguer V, Walsh TJ, Hope W, Cortez KJ: **Galactomannan antigen detection in the diagnosis of invasive aspergillosis**. *Expert Review of Molecular Diagnostics* 2007, **7**:21–32.

75. Blijlevens NMA, Donnelly JP, Meis JFGM, Verweij PE, de Pauw BE: **Aspergillus galactomannan antigen levels in allogeneic haematopoietic stem cell transplant recipients given total parenteral nutrition**. *Transpl Infect Dis* 2002, **4**:64–65.

76. Ortiz-Brizuela E, Rangel-Cordero A, Ponce-de-León A, Sierra-Madero J: **False-positive results in the galactomannan Platelia™ Aspergillus assay with generic piperacillin/tazobactam**. *Revista Iberoamericana de Micología* 2019, **36**:51–52.

77. Mikulska M, Furfaro E, Viscoli C: **Non-cultural methods for the diagnosis of invasive fungal disease**. *Expert Review of Anti-infective Therapy* 2015, **13**:103–117.

78. Sulahian A, Porcher R, Bergeron A, Touratier S, Raffoux E, Menotti J, Derouin F, Ribaud P: **Use and Limits of (1-3)-β- D -Glucan Assay (Fungitell), Compared to Galactomannan Determination (Platelia Aspergillus), for Diagnosis of Invasive Aspergillosis**. *J Clin Microbiol* 2014, **52**:2328–2333.

79. Aubry A, Porcher R, Bottero J, Touratier S, Leblanc T, Brethon B, Rousselot P, Raffoux E, Menotti J, Derouin F, et al.: **Occurrence and kinetics of false-positive Aspergillus galactomannan test results following treatment with beta-lactam antibiotics in patients with hematological disorders**. *J Clin Microbiol* 2006, **44**:389–394.

80. Vergidis P, Razonable RR, Wheat LJ, Estes L, Caliendo AM, Baden LR, Wingard JR, Baddley J, Assi M, Norris S, et al.: **Reduction in False-Positive Aspergillus Serum Galactomannan Enzyme Immunoassay Results Associated with Use of Piperacillin-Tazobactam in the United States**. *J Clin Microbiol* 2014, **52**:2199–2201.

81. Racil Z, Kocmanova I, Lengerova M, Winterova J, Mayer J: **Intravenous PLASMA-LYTE as a Major Cause of False-Positive Results of Platelia Aspergillus Test for Galactomannan Detection in Serum**. *Journal of Clinical Microbiology* 2007, **45**:3141–3142.

82. Surmont I, Stockman W: **Gluconate-Containing Intravenous Solutions: Another Cause of False-Positive Galactomannan Assay Reactivity**. *J Clin Microbiol* 2007, **45**:1373–1373.

83. Nguyen MH, Jaber R, Leather HL, Wingard JR, Staley B, Wheat LJ, Cline CL, Baz M, Rand KH, Clancy CJ: **Use of Bronchoalveolar Lavage To Detect Galactomannan for Diagnosis of Pulmonary Aspergillosis among Nonimmunocompromised Hosts**. *J Clin Microbiol* 2007, **45**:2787–2792.

84. Upton A, Gugel A, Leisenring W, Limaye A, Alexander B, Hayden R, Marr KA: **Reproducibility of Low Galactomannan Enzyme Immunoassay Index Values Tested in Multiple Laboratories**. *J Clin Microbiol* 2005, **43**:4796–4800.

85. Penack O, Rempf P, Graf B, Blau IW, Thiel E: **Aspergillus galactomannan testing in patients with long-term neutropenia: implications for clinical management**. *Annals of Oncology* 2008, **19**:984–989.

86. **NCCLS. Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition**. NCCLS document EP5-A2 [ISBN 1-56238-542-9]. NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA; 2004.

87. Ascioglu S, Rex JH, de Pauw B, Bennett JE, Bille J, Crokaert F, Denning DW, Donnelly JP, Edwards JE, Erjavec Z, et al.: **Defining opportunistic invasive fungal infections in immunocompromised patients with cancer and hematopoietic stem cell transplants: an international consensus**. *Clin Infect Dis* 2002, **34**:7–14.

88. Donnelly JP, Chen SC, Kauffman CA, Steinbach WJ, Baddley JW, Verweij PE, Clancy CJ, Wingard JR, Lockhart SR, Groll AH, et al.: **Revision and Update of the Consensus Definitions of Invasive Fungal Disease From the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium**. *Clinical Infectious Diseases* 2020, **71**:1367–1376.

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(BG)
опасно
Причинява тежки изгаряния на кожата и сериозно увреждане на очите. Може да причини алергична кожна реакция. Вреден за водните организми, с дълготраен ефект.
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. Да се избягва изпускане в околната среда. 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. Škodlivý pro vodní organismy, s dlouhodobými účinky.
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. Zabraňte uvolnění do životního prostředí. 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. Schädlich für Wasserorganismen, mit langfristiger Wirkung.
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. Freisetzung in die Umwelt vermeiden. 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. Skadelig for vandlevende organismer, med langvarige virkninger.
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. Undgå udledning til miljøet. Bortskaffelse af indholdet/beholderen i henhold til de lokale/regionale/nationale/internationale forskrifter.

(EE)
Ettevaatust
Põhjustab rasket nahasöövitust ja silmakahjustusi. Võib põhjustada allergilist nahareaktsiooni. Ohtlik veeorganismidele, pikaajaline toime.
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. Vältida sattumist keskkonda. Sisu/konteineri käitlus vastavuses kohalike/ regionaalsete/rahvuslike/rahvusvaheliste nõuetega.

(EN)
Danger
Causes severe skin burns and eye damage. May cause an allergic skin reaction. Harmful to aquatic life with long lasting effects.
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. Avoid release to the environment. 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. Nocivo para los organismos acuáticos, con efectos nocivos duraderos.
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. Evitar su liberación al medio ambiente. 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. Haitallista vesieliöille, pitkäaikaisia haittavaikutuksia.
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. Vältettävä päästämistä ympäristöön. 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. Nocif pour les organismes aquatiques, entraîne des effets néfastes à long terme.
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. Éviter le rejet dans l'environnement. 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. Επιβλαβές για τους υδρόβιους οργανισμούς, με μακροχρόνιες επιπτώσεις.
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. Να αποφεύγεται η ελευθέρωση στο περιβάλλον. Απορρίψτε τα περιεχόμενα/δοχείο σύμφωνα με τους τοπικούς/εθνικούς/διεθνείς κανονισμούς.

(HR)

Opasnost

Uzrokuje teške opekline kože i ozljede oka. Može izazvati alergijsku reakciju na koži. Štetno za vodeni okoliš s dugotrajnim učincima.
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. Izbjegavati ispuštanje u okoliš. Odložite sadržaje /spremnike u skladu s lokalnim/regionalnim/nacionalni/međunarodnim odredbama.

(HU)

Veszély

Smarkiai nudegina odą ir pažeidžia akis. Allergiás bőrreakciót válthat ki. Ártalmas a vízi élővilágra, hosszan tartó károsodást okoz.
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. Kerülni kell az anyagnak a környezetbe való kijutását. 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. Nocivo per gli organismi acquatici con effetti di lunga durata.
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. Non disperdere nell'ambiente. 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. Kenksminga vandens organizmams, sukelia ilgalaikius pakitimus. 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. Saugoti, kad nepatektų į aplinką. Turinį/talpą išpilti (išmesti) - šalinti pagal vietines / regionines / nacionalines / tarptautines taisykles.

(LV)

Briesmas

Smarkiai nudegina odą ir pažeidžia akis. Gali sukelti alerginę odos reakciją. Kenksminga vandens organizmams, sukelia ilgalaikius pakitimus. 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. Saugoti, kad nepatektų į aplinką. Turinį/talpą išpilti (išmesti) - šalinti pagal vietines / regionines / nacionalines / tarptautines taisykles.

(NL)

Gevaar

Veroorzaakt ernstige brandwonden en oogletsel. Kan een allergische huidreactie veroorzaken. Schadelijk voor in het water levende organismen, met langdurige gevolgen.
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. Voorkom lozing in het milieu. De inhoud en de verpakking verwerken volgens de plaatselijke/regionale/nationale/internationale voorschriften.

(NO)

Fare

Forårsaker alvorlige hudforbrenninger og øyeskader. Kan forårsake allergiske hudreaksjoner. Skadelig for vannlevende organismer, langtidsvirkning
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. Unngå utslipp til miljøet. 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. Działa szkodliwie na organizmy wodne, powodując długotrwałe skutki.
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. Unikać uwolnienia do środowiska. 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. Nocivo para os organismos aquáticos com efeitos duradouros.
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. Evitar a libertação para o ambiente. 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. Nociv pentru mediul acvatic cu efecte pe termen lung.

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. Evitaţi dispersarea în mediu. Aruncaţi conţinutul/ containerul în acord cu regulamentele locale/ regionale/naţionale/internaţionale.

(SE)

Fara
Orsakar allvarliga frätskador på hud och ögon. Kan orsaka allergisk hudreaktion. Skadliga långtidseffekter för vattenlevande organismer. 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. Undvik utsläpp till miljön. Innehållet / behållaren avfallshanteras enligt lokala / regionala / nationella / internationella föreskrifter.

(SL)

Nevarno
Povzroča hude opekline kože in poškodbe oči. Lahko povzroči alergijski odziv kože. Škodljivo za vodne organizme, z dolgotrajnimi učinki. 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 ZAUŽITJU: izprati usta. NE izzvati bruhanja. 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. Preprečiti sproščanje v okolje. 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. Škodlivý pre vodné organizmy, s dlhodobými účinkami. Noste ochranné rukavice/ochranný odev/ochranné okuliare/ochranu tváre. PO ZASIAHNUTÍ OČÍ: Niekoľko minút ich opatrne vyplachujte vodou. Ak používate kontaktné šošovky a ak je to možné, odstráňte ich. Pokračujte vo vyplachovaní. 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. Zabráňte uvoľneniu do životného prostredia. Zneškodnenie obsahu/obalu v súlade s miestnymi/oblastnými/národnými/medzinárodnými nariadeniami.

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