PLATELIA™ *ASPERGILLUS* Ag

1 plate - Σ 96 REF 62794

The Platelia™ *Aspergillus* Ag is an immunoenzymatic sandwich microplate assay for the detection of *Aspergillus galactomanna*n antigen in serum and bronchoalveolar lavage (BAL) fluid

IVD CE

881115 - 2013/10

BIO-RAD

CONTENTS

1- INTENDED USE

The Platelia™ *Aspergillus* Ag is an immunoenzymatic sandwich microplate assay for the detection of *Aspergillus* galactomannan antigen in adult and pediatric serum samples and bronchoalveolar lavage (BAL) fluid samples.

The Platelia™ *Aspergillus* Ag is a test which, when used in conjunction with other diagnostic procedures such as microbiological culture, histological examination of biopsy samples and radiographic evidence can be used as an aid in the diagnosis of Invasive Aspergillosis.

2- INDICATIONS FOR USE

The Platelia™ *Aspergillus* Ag is an immunoenzymatic sandwich microplate assay for the detection of *Aspergillus* galactomannan antigen in adult and pediatric serum samples and bronchoalveolar lavage (BAL) fluid samples.

The Platelia™ *Aspergillus* Ag is a test which, when used in conjunction with other diagnostic procedures such as microbiological culture, histological examination of biopsy samples and radiographic evidence can be used as an aid in the diagnosis of Invasive Aspergillosis.

3- SUMMARY AND EXPLANATION

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 on the increase for the past 10 years, constitute the most serious infections. They mainly occur in neutropenic patients (following anti-cancer treatment) and in patients treated with immunosuppressants (organ transplantations, particularly bone marrow transplantation) and corticosteroids [10].

Aspergillus is rarely isolated from blood culture. The diagnosis is often based on nonspecific diagnostic or radiological evidence (clinical symptoms, CT scan, chest x-ray, etc.)

The test for soluble galactomannan antigen in serum appears to be a serological method able to aid in the diagnosis of Invasive Aspergillosis [9, 12, 23, 54, 62].

In addition, for Solid Organ Transplant recipients, detection of galactomannan antigen in bronchoalveolar lavage (BAL) has proven to be advantageous for the diagnosis of invasive aspergillosis in this population [8,17,18].

4- PRINCIPLE OF THE PROCEDURE [45]

The Platelia™ *Aspergillus* Ag is a one-stage immunoenzymatic sandwich microplate assay which detects galactomannan in human serum and BAL fluid. The assay uses rat EBA-2 monoclonal antibodies, which are directed against *Aspergillus* galactomannan, and have been characterized in previous studies [25, 46]. The monoclonal antibodies are used, (1) to coat the wells of the microplate and bind the antigen, and (2) to detect the antigen bound to the sensitized microplate (conjugate reagent: peroxidase-linked monoclonal antibodies). Serum or BAL fluid samples 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 [24]. The treated samples and conjugate are added to the wells coated with monoclonal antibodies, and incubated. A monoclonal antibody - galactomannan - monoclonal antibody / peroxidase complex is formed in the presence of galactomannan 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 color reaction. The enzyme reaction is stopped by the addition of acid, which changes the blue color to yellow. The absorbance (optical density) of specimens and controls is determined with a spectrophotometer set at 450 and 620/630 nm wavelength.

5- REAGENTS

Platelia™ *Aspergillus* Ag: product No. 62794 (96 Tests)

Store the kit at 2-8°C. Bring all reagents to room temperature (18-25°C) **for at least 30 minutes** before use. Return all reagents to 2-8°C immediately after use. Return unused strips/plates to pouch and reseal.

Do not remove desiccant. After dilution, Working washing solution can be kept for 14 days at 2-30°C. All other reagents except Concentrated Washing Solution (R2) and Stop Solution (R10) should be used within 8 weeks of opening. The Concentrated Washing Solution (R2) and Stop Solution (R10) are stable until expiration after opening. Reagents are supplied in sufficient quantity to perform 96 tests in a maximum of 9 batches.

Component		Contents	Quantity
R1	**Microwell Strip Plate**	**Microplate:** - 96 wells (12 strips of 8 wells each) coated with anti-galactomannan monoclonal antibodies - Strip tabs labeled "85"	1 Plate / 12 x 8 Wells
R2	**Concentrated Washing Solution (20X)**	**Concentrated Washing Solution (20X):** - Tris NaCl buffer (pH 7.4) - 2% Tween® 20 - Preservative: 0.04 % ProClin™ 300	1 x 70 mL
R3	**Negative Control Serum**	**Negative Control Serum:** - Human negative serum - Negative for anti-HIV-1, anti-HIV-2, anti-HCV antibodies and HBs Ag - Preservative: 0.3% ProClin™ 300	2 x 1.7 mL
R4	**Cut-off Control Serum**	**Cut-off Control Serum:** - Human serum containing *galactomannan* - Negative for anti-HIV-1, anti-HIV-2, anti-HCV antibodies and HBs Ag - Preservative: 0.3% ProClin™ 300	2 x 1.7mL
R5	**Positive Control Serum**	**Positive Control Serum:** - Human serum containing *galactomannan* - Negative for anti-HIV-1, anti-HIV-2, anti-HCV antibodies and HBs Ag - Preservative: 0.3% ProClin™ 300	2 x 1.7 mL
R6	**Conjugate**	**Conjugate (ready to use):** - Anti- *galactomannan* monoclonal antibody / peroxidase labeled - Preservative: 0.3% ProClin™ 300	1 x 8 mL
R7	**Sample Treatment Solution**	**Sample Treatment Solution (ready to use):** - EDTA acid solution	1 x 13 mL
R9	**Chromogen: TMB Solution**	**Chromogen TMB Solution (ready to use):** - 3,3',5,5'-tetramethylbenzidine* (<0.1%) - H_2O_2 (<1.0 %)	1 x 28 mL
R10	**Stopping Solution**	**Stopping Solution (ready to use):** - 1 N sulphuric acid solution (H_2SO_4)	1 x 28 mL

****Note***: TMB (3,3',5,5'-tetramethylbenzidine) is a non-carcinogenic and non-mutagenic chromogen for peroxidase.

6- WARNINGS FOR USERS

1. For *in vitro* diagnostic use.
2. For professional use only.
3. Use of this test kit with samples other than human serum and BAL fluid is not recommended.
4. The Positive Control, Cut-off Control, and Negative Control are manufactured from human serum that has been tested and found to be non-reactive for HBsAg and antibodies to HIV-1, HIV-2 and HCV with CE marked tests. However, all reagents should be handled as though capable of transmitting infection. All tests should be conducted in accordance with the OSHA Standard on Bloodborne Pathogens, Biosafety Level 2 or other appropriate biosafety practices.
5. Wear protective clothing, including lab coat, eye/face protection and disposable gloves (synthetic, non-latex gloves are recommended) and handle the kit reagents and patient samples with the requisite Good Laboratory Practices. Wash hands thoroughly after performing the test.
6. Do not pipette by mouth.
7. Do not smoke, drink, or eat in areas where specimens or kit reagents are being handled.
8. Avoid splashing samples or solutions
9. Biological spills not containing acid should be wiped thoroughly with an effective disinfectant. Disinfectants that can be used include (but are not limited to) a solution of 10% bleach (0.5% solution of sodium hypochlorite), 70% ethanol, or 0.5% Wescodyne Plus™. Materials used to wipe up spills may require biohazardous waste disposal.

   CAUTION: Do not place solutions containing bleach in the autoclave.
10. Spills containing acid should be appropriately absorbed (wiped up) or neutralized with sodium bicarbonate, and the area rinsed and wiped dry; if it contained biohazardous material, wipe the area with one of the chemical disinfectants.
11. Dispose of all specimens and materials used to perform the test as though they contain an infectious agent. Laboratory chemical and biohazardous wastes must be handled and discarded in accordance with all local, regional and national regulations.
12. For hazard and precaution recommendations related to some chemical components in this test kit, please refer to the pictogram(s) mentioned on the labels and the information supplied at the end of instruction for use. The Safety Data Sheet is available on www.bio-rad.com.

7- PRECAUTIONS FOR USERS

1. **FROZEN SERUM OR BAL FLUID SAMPLES STORED IN UNKNOWN CONDITIONS MAY GIVE FALSE POSITIVE RESULTS DUE TO CONTAMINATION WITH FUNGUS AND/OR BACTERIA.**
2. Do not use kit or any kit reagents after the stated expiration date.
3. 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.

**on the vial label*

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***

4. **Bring all reagents to room temperature for at least 30 minutes before use**.
5. Mix thoroughly every reagent before use.
6. Mix thoroughly the Concentrated Washing Solution (R2) before preparing the Working Washing Solution, exercising care to avoid microbial contamination.
7. Do not conduct the test in the presence of reactive vapors (acids, alkalis, aldehydes) or dust, which could affect the enzymatic activity of the Conjugate.
8. For manual pipetting of controls and specimens, use individual pipette tips to prevent carryover of samples.

9. To ensure adequate washing of the wells, comply with the recommended number of wash cycles and ensure that all wells are completely filled and then completely emptied. Washing should not be performed manually with a squeeze bottle.
10. Do not allow the microplate to dry between the end of the wash cycle and addition of reagents.
11. Do not use the same container for the Conjugate and Chromogen TMB Solution.
12. Do not allow Conjugate or Chromogen TMB Solution to come into contact with metal or metallic ions.
13. Avoid exposing the Chromogen TMB Solution to strong light during storage or incubation. Do not allow the chromogen solutions to come into contact with an oxidizing agent.
14. Avoid contact of the Stopping Solution with any oxidizing agent. Do not allow the Stopping Solution to come into contact with metal or metallic ions.
15. Use clean, dust-free materials (tubes, tips, containers, etc.) to minimize the possibility of contamination with *Aspergillus* spores from the environment. Because galactomannan is heat-stable, sterilization of material used does not guarantee the absence of contaminating antigen. Pyrogen-free materials are optimal, but standard material can be used with adequate precautions.
16. Limit exposure of solutions (sera, BAL fluid, Sample Treatment Solution, Conjugate) or open containers (plates, tubes, pipettes) to the air.
17. Do not pour any unused Conjugate back into the original container.
18. The Chromogen TMB Solution must be colorless. The appearance of a blue color indicates the reagent is contaminated and should not be used.

8- REAGENT PREPARATION AND STORAGE

Microwell Strip Plate (R1)

Every frame containing 12 strips is packaged in a pouch. Cut open the pouch using scissors just below the joint. Open the pouch and take out the frame. Put the frame containing the unused strips back in the original pouch. **Carefully reseal the pouch** and store at +2-8°C.

After the vacuum-packed pouch has been opened, the strips stored at +2-8°C in their original pouch that has been carefully resealed are stable for 8 weeks. Check whether the desiccant is still present.

Washing Solution (R2)

Prepare Working Washing Solution as needed by adding one part Concentrated Washing Solution (R2) to 19 parts deionized or distilled water. The Working Washing Solution can be stored for 14 days at 2-30°C. Prepare a sufficient amount of Working Washing Solution to complete the run (80 mL for one strip: 4 mL R2 + 76 mL distilled water).

After opening, the Concentrated Washing Solution stored at +2-30°C, in the absence of contamination is stable until the expiration date indicated on the label.

Negative Control Serum (R3), Cut-off Control Serum (R4) and Positive Control Serum (R5)

The controls must be heat-treated with the Sample Treatment Solution (R7) as patient specimens, in order to also be a monitor of the treatment.

After opening, these reagents stored at +2-8°C, are stable for 8 weeks, in the absence of contamination.

Conjugate (R6), Sample Treatment Solution (R7), Chromogen: TMB solution (R9)

These reagents are ready to use.

After opening, these reagents stored at +2-8°C are stable for 8 weeks if they are free of contamination.

Stopping reaction (R10)

This reagent is ready to use.

After opening, this reagent stored at +2-8°C is stable until the validity date shown on the label if there is no contamination.

9- SPECIMEN COLLECTION

This test is performed on serum or BAL fluid.

I. SERUM

Collect blood samples according to standard laboratory procedures. Serum samples must be uncontaminated with fungal spores and/or bacteria. Transport and store samples in sealed tubes, unexposed to air. Unopened samples can be stored at 2-8°C for up to 5 days prior to testing. After initial opening, samples may be stored at 2-8°C for 48 hours prior to testing. For longer storage, store the serum at -70°C.

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

The results are not affected by samples containing 20 mg/L of bilirubin, lipemic samples containing the equivalent of 2 g/L of triolein (triglyceride) or hemolyzed samples containing 500 mg/dL of hemoglobin. Interferences related to excess albumin have not been tested.

Do not decomplement sera.

II. BAL FLUID

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

BAL fluid samples must be uncontaminated with fungal spores and/or bacteria. Transport and store samples in sealed tubes, unexposed to air. After initial opening, samples may be stored at 2-8°C for up to 24 hours. For longer storage, store the BAL samples frozen (-20°C or less) up to 5 months.

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

10- PROCEDURE

Materials provided

See REAGENTS section.

Materials required but not provided

1. Distilled or deionized water, for dilution of Concentrated Washing Solution.
2. Absorbent paper.
3. Disposable gloves.
4. Protective glasses.
5. Sodium hypochlorite (bleach) and sodium bicarbonate.
6. Pipettes or multipipettes, adjustable or fixed, to measure and dispense 50 µL, 100 µL, 300 µL, and 1000 µL.
7. 1.5 mL polypropylene microcentrifuge tubes with airtight stoppers, able to support heating to 120°C (heat block) or 100°C (boiling water bath):
   - Screw caps and tubes: 1.5 mL Conical Tubes,

   OR
   - Snap cap tubes: EZ Micro Test Tubes, 1.5 mL,
   - Micro-tube cap locks, these locks securely seal snap cap tubes by preventing caps from opening during temperature and pressure changes and also allow tubes to be easily lifted out of heat block or boiling water bath.
8. Laboratory bench centrifuge for 1.5 mL polypropylene tubes capable of obtaining 10,000g (Brinkman Cat. # 22-36-280-1 or VWR Scientific Cat. # 20901-051 or equivalent).
9. **If heat block is used for the treatment of the sera/BAL fluid**:
   - Heat block. The following heat block models are recommended:
   - Single block model: Grant Cat. # QBD-1L - outside of the US: Grant Cat. # QBD1 distributed by VWR under Cat. # 460-0074)

- Two block model: Grant Cat. # QBD-2L – outside of the US: Grant Cat. # QBD2 distributed by VWR under Cat. # 460-0076)
- Block for heat blocks: both heat blocks (QBD-1L, QBD1 and QBD-2L, QBD2) must be used with Grant block Cat. # QB-E1 distributed outside of the US by VWR under Cat. # 460-8517

If boiling water is used for the treatment of the sera/BAL fluid:

- Round, floating micro-centrifuge rack for a 1 L beaker (in the US: VWR Scientific Cat. # 60986-100 or Nalgene Cat # 5974-1015 or equivalent).
- Boiling water bath at 100°C.

10. Vortex agitator.
11. Microplate incubator at 37 ± 1°C.
12. Semi-automated or automated microplate washer.
13. Microplate reader equipped with 450 nm and 620/630 nm filters.

Procedural Comments

Negative, Positive, and Cut-off Controls must be tested on each run to validate the test results.

Treatment of the sera/BAL Fluid

All control sera: negative (R3), cut-off (R4) and positive (R5) must be processed at the same time as serum/BAL fluid samples:

1. Pipette 300 µL of each test serum/BAL fluid and control into individual 1.5 mL polypropylene tube.
2. Add 100 µL of Sample Treatment Solution (R7) to each tube.
3. Mix tubes thoroughly by vigorous mixing or vortexing to mix thoroughly. Tightly close the tube to prevent opening during heating,
4. **Heat block option:**
   Heat tubes for **6 minutes in a heat block at 120°C**. Tubes must be placed in the block only when the prescribed temperature is reached (*).
   OR
   Water bath option:
   If using a boiling water bath: heat tubes for **3 minutes at 100°C** (*). Tubes must be placed in the water bath only when the prescribed temperature is reached.
5. Carefully remove hot tubes from the heat block or the boiling water bath and place in a centrifuge. Centrifuge tubes at 10,000 x g for 10 minutes. The supernatant is used for the detection of the galactomannan antigen.
6. Test the supernatants using the following procedure. After preparation, the supernatant may be removed and stored at 2-8°C for up to 48 hours prior to testing. If analysis of the results indicates retesting is required, another aliquot of the sample must be treated for testing.

(*) Strict compliance with the prescribed temperature and the prescribed turn-around time as well as use of recommended materials are essential for success of the test.

Do not rely on the temperature displayed by the apparatus, please check that the temperature complies with specifications by using a calibrated thermometer which will be 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.

EIA Procedure

Strictly comply with the proposed protocol.

Comply with Good Laboratory Practice.

1. **Bring reagents to room temperature (+18-25°C) for at least 30 minutes before use**.
2. Prepare the Working Washing Solution.
3. Prepare a chart for identification of test sera/BAL fluid Samples 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										

4. Remove the plateholder and microwell strips (R1) from the plate pouch. Return any strips that will not be used to the pouch, with the desiccant, and reseal the pouch.
5. Mix the contents of the Conjugate bottle (R6) 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 designated above. Do not add serum/BAL fluid samples to the wells before the conjugate.
6. **Cover plate with plate sealer**, or other means to prevent evaporation, ensuring that entire surface is covered and watertight.
7. Incubate the microplate in a dry microplate incubator for 90 ± 5 minutes at 37°C (± 1°C).
8. 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 remaining liquid.
9. Rapidly add 200 µL of the Chromogen TMB (R9) Solution to each well, avoiding exposure to bright light.
10. Incubate the microplate in the dark at room temperature (+18-25°C) for 30 ± 5 minutes. **Do not use adhesive film during this incubation step**.
11. Add 100 µL of Stopping Solution (R10) to each well, utilizing the same order for addition of Chromogen TMB Solution. Mix well.
12. Thoroughly wipe the bottoms of each plate.
13. Read the optical density of each well at 450 nm (reference filter of 620/630 nm). Microplates must be read **within 30 minutes** of addition of Stopping Solution.

11- QUALITY CONTROL (VALIDITY CRITERIA)

Cut-off Control: The O.D. of each Cut-off Control Serum must be
≥ 0.300 and ≤ 0.800.

Positive Control: The index of the Positive Control Serum must be greater than 1.50.

$$I = \frac{\text{OD Positive Control (R5)}}{\text{Mean Cut-off Control OD}} > 1.50$$

Negative Control: The index of the Negative Control Serum must be less than 0.40.

$$I = \frac{\text{OD Negative Control (R3)}}{\text{Mean Cut-off Control OD}} < 0.40$$

Failure of any of the controls to meet the validity 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 sample should be used in the repeat assay.

Example Calculation:

Sample	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 together and divide the result by 2:

(0.513 + 0.533) ÷ 2 = 0.523

Negative Control Index

To calculate the index of the Negative Control, divide the OD of the Negative Control by the mean Cut-off Control OD:

$$I = \frac{0.116}{0.523} = 0.22$$

Positive Control Index

To calculate the index of the Positive Control, divide the OD of the Positive Control by the mean Cut-off Control OD:

$$I = \frac{1.834}{0.523} = 3.51$$

Validity

In the above example:

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

12- INTERPRETATION OF RESULTS

The presence or absence of galactomannan antigen in the test sample 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 optical density:

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

Calculation of an index (I) for each test sample:

Calculate the following ratio for each test sample:

$$I = \frac{\text{OD sample}}{\text{Mean Cut-off Control OD}}$$

Interpretation of sera/BAL fluid with an index < 0.50:

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

For all positive patients, it is recommended that a new aliquot of the same sample (serum/BAL) be repeated.

Note: 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 samples of high-risk patients is recommended to increase the sensitivity and early positivity of the test.

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

Example Calculation:

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

Calculations

Refer to the Quality Control (Validity 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 together and divide the result by 2:

(0.513 + 0.533) ÷ 2 = 0.523

Patient Sample #1

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

$$I = \frac{0.134}{0.523} = 0.26$$

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

Patient Sample #2

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

$$I = \frac{0.436}{0.523} = 0.83$$

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

Patient Sample #3

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

$$I = \frac{1.196}{0.523} = 2.29$$

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

Please refer to Interpretation of Positive Results in Section 12.

13- LIMITATIONS OF THE PROCEDURE

1. **A negative test from serum and/or BAL samples cannot rule out the diagnosis of Invasive Aspergillosis. Serum samples from patients at risk for Invasive Aspergillosis should be tested twice a week.**
2. The Platelia™ *Aspergillus* Ag Procedure and the Interpretation of Results must be followed when testing samples for the presence of galactomannan antigen. The user of the kit is advised to read the package insert carefully prior to conducting the test. In particular, the test procedure must be carefully followed for sample and reagent pipetting, plate washing, and timing of the incubation steps.
3. Failure to add specimen or reagent as instructed in the procedure could result in a falsely negative test. **Repeat testing of additional samples should be considered where there is clinical suspicion of Invasive Aspergillosis or procedural error**.
4. 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.
5. The performance of the Platelia™ *Aspergillus* Ag has not been evaluated with neonatal samples. There is a higher incidence in the number of false positive galactomannan results reported in the European literature in samples from neonatal population [13, 15, 33, 44].
6. The Platelia™ *Aspergillus* Ag may exhibit reduced detection of galactomannan in patients with chronic granulomatous disease (CGD) and Job's syndrome [56, 58].
7. The concomitant use of mold-active anti-fungal therapy in some patients with Invasive Aspergillosis may result in reduced sensitivity with the Platelia™ *Aspergillus* Ag [30, 31].
8. The Platelia™ *Aspergillus* Ag has not been evaluated for use with plasma or other sample types such as urine or CSF.
9. The performance of the Platelia™ *Aspergillus* Ag has not been established for manual reading and/or visual result determination.
10. Other genera of fungi such as *Penicillium, Alternaria Paecilomyces, Geotrichum* and *Histoplasma* have shown reactivity with rat, EBA-2 monoclonal antibodies used in the assay for the detection of *Aspergillus* galactomannan. Histoplasmosis should be considered in endemic areas including parts of the United States [36, 50, 59].
11. Cross-reactivity of BAL fluid samples with *Mycoplasma pneumoniae* or anaesthetic drugs/lubricants used to numb the neck/throat area for the aspiration process has not been evaluated.
12. Positive reactions with no clinical signs:

    The following should be considered with regard to the early galactomannan antigen detection in serum or BAL before the appearance of clinical and/or radiological signs. Positive test results without clinical signs are usually 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 [30].

    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 [44]. Although some of these cases could be related to real circulation of *Aspergillus* antigens, most cases can be considered to be false-positives [7].
    b. Galactofuranose has been demonstrated in various foods, particularly cereals, cereal products and cream desserts [1, 27]. Unlike human milk, cow's milk formulas frequently contain high concentrations of galactomannan [13]. Dietary factors must therefore be taken into account in interpretation of the course of antigenemia in young children, and more generally in all patients with an altered intestinal barrier [6, 13]. 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 galactomannan test results in patients receiving piperacillin/ tazobactam. There have also been reports of certain lots or batches of piperacillin/ tazobactam that have been found to be positive for galactomannan antigen. Therefore, positive test results in patients receiving piperacillin / tazobactam should be interpreted cautiously and confirmed by other diagnostic methods. Detection of galactomannan has also been reported in some batches of amoxicillin associated with clavulanic acid parenteral preparations. Therefore, semi-synthetic ß-lactam treatments should be taken into account when interpreting the test [1, 3, 32].

   Nevertheless, as Platelia™ *Aspergillus* Ag can detect galactomannan antigen well before clinical or radiological signs appear, the occurrence of Invasive Aspergillosis cannot be ruled out. Therefore, patients treated with piperacillin/tazobactam with positive test results should be followed carefully.

d. Positive reactions in the absence of clinical signs may be observed in patients receiving products containing galactomannan, either parenterally or orally (in the presence of an alteration of the intestinal barrier). The presence of galactomannan in these products can often be explained by the use of a fermentation process based on fungal microorganisms. A positive result will not be observed in a patient, however, unless the serum concentration of exogenous galactomannan reaches or exceeds the test's detection threshold.

   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 [14, 41, 49].

13. There have been reports of positive reactions for galactomannan in serum and bronchoalveolar lavage fluid associated with PLASMA-LYTE™ have been observed in several studies [14, 41]. Therefore, any administration of PLASMA-LYTE™ should be taken into account when interpreting the results of this test.
14. The results of the Platelia™ *Aspergillus* Ag in Bronchoalveolar Lavage (BAL) fluid samples from non-immunocompromised patients should be interpreted with caution. [37]
15. 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 grey zone is included in the result interpretation of the assay.
16. In addition, results of the Platelia™ *Aspergillus* Ag in Bronchoalveolar Lavage (BAL) fluid samples between 0.5-1.0 index have a lower predictive value than BAL sample results > 1.0 index values, hence the results between 0.5-1.0 index values should be reviewed and supported by other clinical, radiological or laboratory evidence of invasive aspergillosis [8, 17].

14- EXPECTED VALUES

I. SERUM

The expected prevalence of Invasive Aspergillosis varies with the patient population; rates from 5-20% have been reported [10, 16].

The following results have been obtained from clinical studies conducted on pediatric (age ≤ 21 years) patients in the United States and on adult patients in North America.

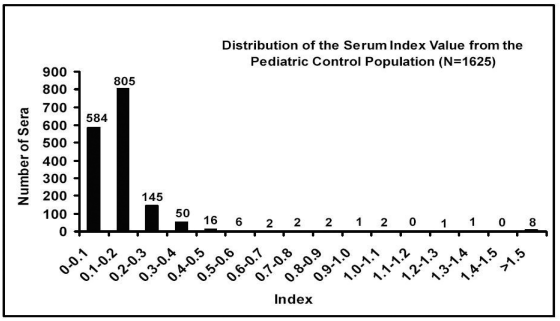
A-Pediatrics

A clinical study was conducted on a total of 1954 serum samples from 129 immunocompromised pediatric (Age ≤ 21 years) patients, at high risk for Invasive Aspergillosis (IA) and patients diagnosed with Proven and Probable Invasive Aspergillosis, at three testing centers in the United States to determine the performance characteristics of the Platelia™ *Aspergillus* Ag. The distribution of index values for these populations is shown in the following charts:

Pediatric Patients diagnosed without Invasive Aspergillosis (control population)

Figure 1

A total of 1625* pediatric serum samples obtained from 108 immuno-compromised pediatric patients at three testing centers in the United States were tested to determine the performance characteristics of the Platelia™ *Aspergillus* Ag. The distribution of index values for samples is shown in the following chart:

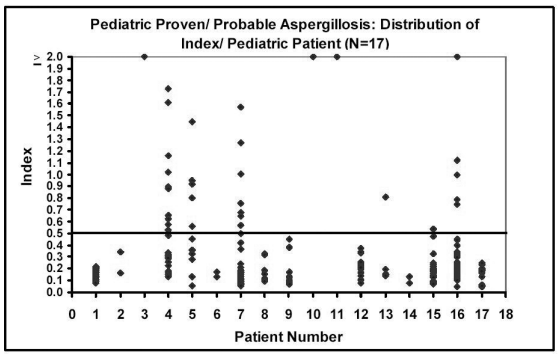


**** Note: 80 samples, from 4 control patients with positive galactomannan antigen results coinciding with piperacillin/tazobactam (Zosyn®) therapy were excluded.***

Pediatric Patients diagnosed with Invasive Aspergillosis

Figure 2

The scatter plot depicts galactomannan assay results for the 249 serum samples from 17 patients in this study diagnosed with proven or probable Invasive Aspergillosis as defined by EORTC/NIAID definitions. Not every serum sample from each patient is expected to be positive. The expected prevalence of Invasive Aspergillosis varies with the patient population; rates from 5-20% have been reported [10, 24]. The prevalence rate of this study was 13.6%.



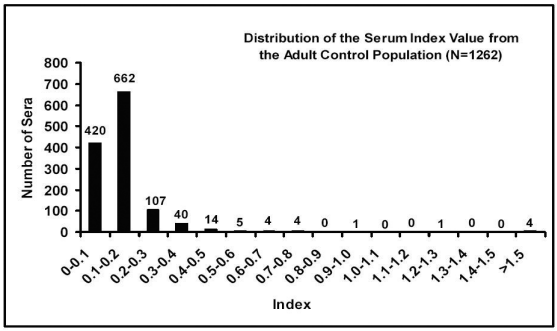
B. Adults

A clinical study was conducted on a total of 1724 serum samples from 172 bone marrow transplant (BMT) and leukemic patients diagnosed with and without Invasive Aspergillosis, at three testing centers in North America to determine the performance characteristics of the Platelia™ *Aspergillus* Ag. The distribution of index values for these populations is represented in the following charts.

Adult Patients diagnosed without Invasive Aspergillosis (control population)

Figure 3

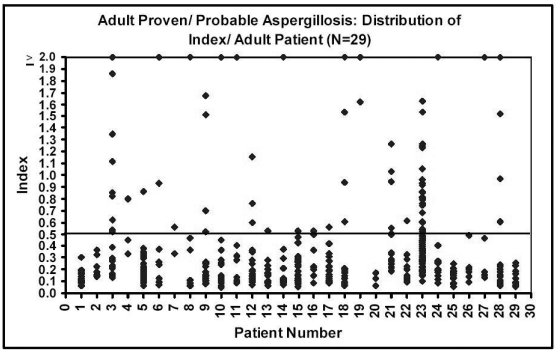
A total of 1262 serum samples obtained from 143 bone marrow transplant (BMT) and leukemic patients at three testing centers in North America were tested with the Platelia™ *Aspergillus* Ag test. The distribution of index values is shown in the following chart.



Adult Patients diagnosed with Invasive Aspergillosis

Figure 4

This scatter plot depicts galactomannan assay results for the 462 serum samples from 29 patients in this study diagnosed with proven or probable Invasive Aspergillosis as defined by EORTC/NIAID definitions. Not every serum sample from each patient is expected to be positive. The expected prevalence of Invasive Aspergillosis varies with the patient population; rates from 5-20% have been reported [10, 24]. The prevalence rate for this study was 16.9%.



The following graphs represent examples of a patient without clinical signs or symptoms of Invasive Aspergillosis (negative for *Aspergillus*) and a patient with proven or probable Invasive Aspergillosis (positive for *Aspergillus*) respectively.

Figure 5

Negative patient:

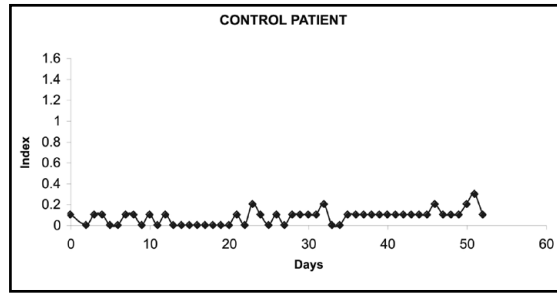
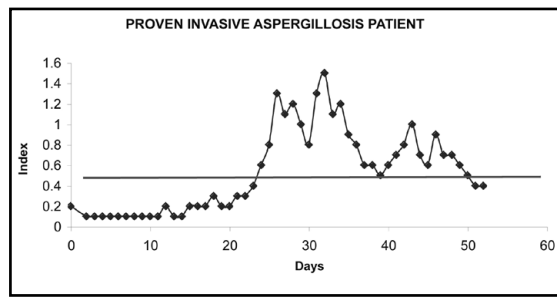


Figure 6

Positive patient:



II. BAL FLUID

Two studies were conducted on a total of 449 BAL samples from 178 Solid Organ transplant (SOT) and lung transplant recipients with and without invasive aspergillosis in the United States to determine the performance characteristics of the Platelia™ *Aspergillus* Ag kit with Bronchoalveolar Lavage Fluid samples.

Of these, there were 403 BAL samples from 167 solid organ and lung transplant recipients without invasive aspergillosis.

In addition, a retrospective analysis was performed on BAL samples from 99 evaluable high risk haematology patients in a study outside the United States which included 58 patients with proven or probable invasive aspergillosis.

Expected values in BAL samples from the combined SOT and lung transplant recipients without Invasive Aspergillosis are presented in the table below. Results are presented by samples from transplant recipients with and without mold colonization.

Table 1
Expected Values by Sample
Combined SOT and Lung Transplant Recipients without Invasive Aspergillosis
N =403 BAL Fluids

Diagnosis	N	Positive (%)	Negative (%)
Controls without colonization	341	11/341 (3.2%)	330/341 (96.8%)
Controls with colonization	62	12/62 (19.4%)	50/62 (80.6%)
Control Total	403	23/403 (5.7%)	380/403 (94.3%)

Expected values in BAL samples from the combined SOT and lung transplant recipients without Invasive Aspergillosis are presented by transplant type in the table below.

Table 2
Expected Values by Sample
Combined SOT and Lung Transplant Recipients without Invasive Aspergillosis By Transplant Type
N =403 BAL Fluids

Transplant Type	N	Positive (%)	Negative (%)
Heart	28	3/28 (10.7%)	25/28 (89.3%)
Kidney	25	3/25 (12.0%)	22/25 (88.0%)
Liver	23	1/23 (4.3%)	22/23 (95.7%)
Lung	327	16/327 (4.9%)	311/327 (95.1%)
Control Total	403	23/403 (5.7%)	380/403 (94.3%)

Expected values were also evaluated in a total of 41 BAL fluid samples from 41 hematological disease patients without Invasive Aspergillosis and are presented in the Table below

Table 3
Expected Values by Sample
Hematologic disease patients without Invasive Aspergillosis
N =41 BAL Fluids

Diagnosis	N	Positive (%)	Negative (%)
Control	41	8/41 (19.5%)	33/41 (80.5%)

15. SPECIFIC PERFORMANCE CHARACTERISTICS

A. REPRODUCIBILITY

a) Reproducibility Studies In Serum

Inter-assay and Intra-assay variability for the Platelia™ *Aspergillus* Ag were determined in a study using a panel of 6 pooled patient serum samples (one negative, one low positive, two positive, and two high positive) obtained at three clinical trial sites in North America. Each of the 6 panel members were tested in triplicate (x3) on 3 different days, on one lot, at two sites (total number of replicates at each site = 9). Each of the 6 panel members was tested in duplicate (x2) on 3 different days, on 1 lot, at a third site (total number of replicates at the third site = 6). One (1) operator performed all precision testing at each site. The data were analyzed according to the Clinical Laboratory Standards Institute (CLSI) (formerly National Committee for Clinical Laboratory Standards (NCCLS)). The mean optical density (OD) and mean index value, standard deviation (SD), percent coefficient of variation (%CV), within run precision (intraassay) and within site (inter-assay) precision for each panel member at each site are illustrated below in the following tables.

Table 4

Site 1

Panel Member	Neg		Low Pos		Pos #1		Pos #2		High Pos#1		High Pos #2		Neg Control		CO Control		Pos Control	
	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index
N	9	9	9	9	9	9	9	9	9	9	9	9	3	3	6	6	3	3
Mean	0.052	0.09	0.445	0.74	0.702	1.17	0.931	1.563	1.227	2.06	2.887	4.83	0.046	0.08	0.606	1.00	2.216	3.67
Within Run (intra-assay)[1] SD	0.002	0.00	0.022	0.03	0.059	0.09	0.044	0.08	0.051	0.09	0.089	0.17	N/A	N/A	0.02	0.03	N/A	N/A
%CV	N/A	N/A	4.8%	4.4%	8.4%	7.6%	4.7%	5.1%	4.2%	4.4%	3.1%	3.6%	N/A	N/A	3.7%	3.4%	N/A	N/A
Total (inter-assay)[2] SD	0.036	0.04	0.051	0.08	0.070	0.14	0.044	0.25	0.058	0.29	0.169	0.58	N/A	N/A	0.102	0.03	0.317	0.12
%CV	N/A	N/A	11.5%	10.4%	10.0%	11.6%	4.7%	15.7%	4.7%	14.3%	5.9%	11.9%	N/A	N/A	16.9%	2.8%	14.3%	3.3%

Site 2

Panel Member	Neg		Low Pos		Pos #1		Pos #2		High Pos#1		High Pos #2		Neg Control		CO Control		Pos Control	
	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index
N	9	9	9	9	9	9	9	9	9	9	9	9	3	3	6	6	3	3
Mean	0.040	0.10	0.280	0.70	0.364	0.89	0.602	1.49	0.801	2.01	1.361	3.43	0.074	0.18	0.415	1.00	1.197	2.97
Within Run (intra-assay)[1] SD	0.006	0.01	0.041	0.09	0.023	0.07	0.045	0.11	0.046	0.10	0.047	0.11	N/A	N/A	0.00	0.01	N/A	N/A
%CV	N/A	N/A	14.5%	13.0%	6.4%	7.6%	7.5%	7.1%	5.7%	4.8%	3.5%	3.2%	N/A	N/A	1.1%	1.1%	N/A	N/A
Total (inter-assay)[2] SD	0.006	0.03	0.058	0.19	0.083	0.18	0.057	0.28	0.042	0.53	0.079	1.00	N/A	N/A	0.094	0.01	0.068	0.54
%CV	N/A	N/A	20.8%	27.0%	22.7%	19.8%	9.5%	18.7%	5.3%	26.5%	5.8%	29.2%	N/A	N/A	22.7%	0.9%	5.7%	18.2%

Site 3

Panel Member	Neg		Low Pos		Pos #1		Pos #2		High Pos#1		High Pos #2		Neg Control		CO Control		Pos Control	
	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index
N	6	6	6	6	6	6	6	6	6	6	6	6	3	3	6	6	3	3
Mean	0.049	0.10	0.388	0.81	0.652	1.36	0.830	1.73	1.158	2.41	2.378	4.96	0.059	0.12	0.480	1.00	1.652	3.45
Within Run (intra-assay)[1] SD	0.003	0.01	0.009	0.02	0.082	0.17	0.068	0.14	0.094	0.20	0.126	0.25	N/A	N/A	0.028	0.06	N/A	N/A
%CV	N/A	N/A	2.4%	2.4%	12.5%	12.2%	8.2%	8.2%	8.1%	8.2%	5.3%	5.1%	N/A	N/A	5.8%	5.8%	N/A	N/A
Total (inter-assay)[2] SD	0.012	0.03	0.078	0.13	0.068	0.15	0.104	0.25	0.082	0.15	0.111	0.34	N/A	N/A	0.028	0.04	0.056	0.23
%CV	N/A	N/A	20.0%	15.8%	10.5%	11.1%	12.5%	14.3%	7.1%	6.2%	4.7%	6.8%	N/A	N/A	5.8%	4.1%	3.4%	6.6%

N/A = not applicable

[1]NCCLS EP5-A, Vol. 19, No. 2, Page 24, Equation (C2)

[2]NCCLS EP5-A, Vol. 19, No. 2, Page 25, Equation (C3) and Equation (C4)

b) Reproducibility in BAL Fluid

Inter-assay and Intra-assay variability for the Platelia™ *Aspergillus* Ag were determined in a study using a panel of 4 pooled patient BAL samples spiked with purified galactomannan (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 analyzed according to the Clinical Laboratory Standards Institute (CLSI) (formerly National Committee for Clinical Laboratory Standards (NCCLS)). The mean optical density (OD) and mean index value, standard deviation (SD), percent coefficient of variation (%CV), within run precision (intraassay) and within site (inter-assay) precision for each panel member are illustrated below in the following table:

Table 5 - Combined Sites Summary

Summary		Negative		High Negative		Low Positive		Medium Positive		Positive Control		Negative Control	
		N= 60		N=60		N=60		N=60		N=60		N=60	
		OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index
Mean		0.121	0.29	0.214	0.50	0.375	0.88	0.575	1.35	1.580	3.72	0.047	0.11
Within Run (Intra Assay)	SD	N/A	N/A	0.037	0.103	0.035	0.078%	0.029	0.067	0.111	0.265	N/A	N/A
	%CV	N/A	N/A	17.4%	20.5%	9.3%	8.9%	5.0%	5.0%	7.0%	7.1%	N/A	N/A
Total (Inter Assay)	SD	N/A	N/A	0.042	0.095	0.061	0.122	0.070	0.138	0.190	0.438	N/A	N/A
	%CV	N/A	N/A	19.6%	18.9%	16.2%	13.9%	12.2%	10.2%	12.0%	11.8%	N/A	N/A

B. CROSS REACTIVITY

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 samples were tested for cross-reactivity with the Platelia™ *Aspergillus* Ag. A total of 151 sera were tested.

Table 6

Pathology	# Samples 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).

C. CLINICAL TESTING

Clinical studies in North America

I. SERUM SAMPLES

Clinical testing to evaluate the sensitivity, specificity, and predictive value of the Platelia™ *Aspergillus* Ag was conducted on pediatric (age ≤ 21 years) patients at three sites located in the United States and on adult patients at three sites located in North America. The studies were conducted using a total of 1954 serum samples collected from 129 pediatric patients and a total of 1724 serum samples collected from 172 adult patients from the following populations*:

- 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 have defined criteria for diagnosis of Invasive Aspergillosis (IA) in patients with hematologic malignancy or hematopoetic stem cell transplant.[2]

SENSITIVITY

A. Pediatrics

Results from this study have been analyzed in terms of patient sensitivity. Sensitivity testing was conducted using the Platelia™ *Aspergillus* Ag at three sites on a combined total of 17 immunocompromised pediatric patients diagnosed with Proven or Probable Invasive Aspergillosis.

Table 7

Diagnosis	Number of patients	Sensitivity	95% Confidence Interval
Proven Aspergillosis	9	44.4% (4/9)	18.9-73.3%
Probable Aspergillosis	8	62.5% (5/8)	30.6-86.3%
Combined Proven and Probable Aspergillosis	17*	52.9% (9/17)	31.0-73.8%

Note: 8 of the 17 patients gave negative Aspergillus galactomannan antigen results. All of the 8 patients with negative Aspergillus galactomannan antigen results received therapy with multiple antifungal agents. The concomitant use of mold-active anti-fungal therapy in some patients with Invasive Aspergillosis may result in reduced sensitivity [31].

B. Adults

Sensitivity testing was conducted using the Platelia™ *Aspergillus* Ag at three sites on a combined total of 29 Bone Marrow Transplant (BMT) and Leukemia adult patients diagnosed with Proven or Probable Invasive Aspergillosis.

Table 8

Diagnosis	Number of patients	Sensitivity	95% Confidence Interval
Proven Aspergillosis	11	81.8% (9/11)	52.3-94.9%
Probable Aspergillosis	18	77.8% (14/18)	54.8-91.0%
Combined Proven and Probable Aspergillosis	29	79.3% (23/29)	61.6-90.2%

SPECIFICITY

A. Pediatrics

Specificity by pediatric patients

Specificity testing was conducted using the Platelia™ *Aspergilllus* Ag at three sites on a combined total of 108* immunocrompomised pediatric patients without signs of Invasive Aspergillosis (control patients).

Table 9

Site	Number of patients	Specificity	95% Confidence Interval
1	44	86.4 % (38/44)	73.3-93.6%
2	59	86.4 % (51/59)	75.5-93.0%
3	5	100% (5/5)	56.6-100%
Combined Sites	108	87.0% (94/108)	79.4-92.1%

Note: 4 patients with positive galactomannan antigen results coinciding with piperacillin / tazobactam therapy were excluded.

Specificity by pediatric samples

Specificity testing was conducted using the Platelia™ *Aspergilllus* Ag at three sites on a combined total of 1625* samples obtained from 108 immunocrompomised pediatric patients without signs of Invasive Aspergillosis (control patients).

Table 10

Site	Number of patients	Specificity	95% Confidence Interval
1	794	98.9% (785/794)	97.9-99.4%
2	731	97.8% (715/731)	96.5-98.6%
3	100	100% (100/100)	96.3-100%
Combined Sites	1625	98.5% (1600/1625)	97.7-99.0%

Note: 80 samples from 4 patients with positive galactomannan antigen results coinciding with piperacillin / tazobactam therapy were excluded.

B. Adults

Specificity by adult patients

Specificity testing was conducted using the Platelia™ *Aspergillus* Ag at three sites on a combined total of 143 Bone Marrow Transplant (BMT) and Leukemia adult patients without signs of Invasive Aspergillosis (control patients).

Table 11

Site	Number of patients	Specificity	95% Confidence Interval
1	28	78.6% (22/28)	60.5-89.8%
2	77	93.4% (71/77)	84.0-96.4%
3	38	89.5% (34/38)	75.9-95.8%
Combined Sites	143	88.8% (127/143)	82.6-93.0%

Specificity by adult samples

Specificity testing was conducted using the Platelia™ *Aspergillus* Ag at three sites on a combined total of 1262 samples obtained from 143 Bone Marrow Transplant (BMT) and Leukemia adult patients without signs of Invasive Aspergillosis (control patients).

Table 12

Site	Number of samples	Specificity	95% Confidence Interval
1	349	98.0% (342/349)	95.9-99.0%
2	560	98.6% (552/560)	97.2-99.3%
3	353	98.9% (349/353)	97.1-99.6%
Combined Sites	1262	98.5% (1243/1262)	97.7-99.0%

PREDICTIVE VALUE

Positive and negative predictive values have been analyzed for the patient population in this study. Based on the actual average of 13.6% prevalence rate in pediatrics and 16.9% prevalence rate in adults observed in this study, positive and negative predictive values have been calculated as below:

A. Pediatrics

Study Prevalence 13.6%

PPV: 39.1% 95% Confidence Interval: 22.2-59.2%
NPV: 92.2% 95% Confidence Interval: 85.3-96.0%

B. Adults

Study Prevalence 16.9%

PPV: 59.0% 95% Confidence Interval: 43.4-72.9%
NPV: 95.5% 95% Confidence Interval: 90.5-97.9%

The expected prevalence of Invasive Aspergillosis varies with the patient population; rates from 5-20% have been reported [10, 24]. For patient populations on the lower end of the published prevalence, the positive and negative predictive values have been re-calculated using a 5% prevalence rate.

A. Pediatrics

Calculated Prevalence 5%

PPV: 17.6% 95% Confidence Interval: 6.5-39.8%
NPV: 97.2% 95% Confidence Interval: 92.1-99.1%

B. Adults

Calculated Prevalence 5%

PPV: 27.2% 95% Confidence interval: 13.7-46.7%
NPV: 98.8% 95% Confidence Interval: 95.4-99.7%

II. BAL FLUID SAMPLES- PERFORMANCE CHARACTERISTICS

Sensitivity and specificity of the Platelia™ *Aspergillus* Ag with BAL fluid samples were evaluated in two studies in the United States on 116 samples from 62 solid organ transplant recipients and 333 samples from 116 lung transplant recipients and one study outside the United States on 99 samples from 99 high risk hematology patients with and without invasive aspergillosis.

A. Sensitivity

Sensitivity was evaluated in Solid Organ Transplant and Lung Transplant recipients diagnosed with invasive aspergillosis as well as hematologic disease patients diagnosed with invasive aspergillosis according to the EORTC/MSG criteria.

I. Solid Organ Transplant recipients with Invasive Aspergillosis

Of the total of 116 samples from 62 solid organ transplant recipients in one study, sensitivity was evaluated in 5 recipients diagnosed with invasive aspergillosis as shown in the table below.

Table 13

Sensitivity with Platelia™ *Aspergillus* Ag

Proven or Probable Invasive Aspergillosis in Solid Organ Transplant Recipients By Patient

Diagnosis	N	Index ≥ 0.5	Sensitivity	95% Confidence Interval
Proven Aspergillosis	2	2	2/2 (100%)	34.2 - 100%
Probable Aspergillosis	3	3	3/3 (100%)	43.8 - 100%
Combined Proven and Probable Aspergillosis	5	5	5/5 (100%)	56.5 - 100%

Table 14

Sensitivity with Platelia™ *Aspergillus* Ag

Proven or Probable Invasive Aspergillosis in Solid Organ Transplant Recipients By Transplant Type

Transplant Type	N	Index ≥ 0.5	Sensitivity	95% Confidence Interval
Heart	1	1	1/1 (100%)	20.6 - 100%
Kidney	3	3	3/3 (100%)	43.8 - 100%
Liver	1	1	1/1 (100%)	20.6 - 100%
Total	5	5	5/5 (100%)	56.5 - 100%

II. Lung Transplant recipients with invasive aspergillosis

Of the total of 333 samples from 116 lung transplant recipients in another study, sensitivity was evaluated in 6 recipients diagnosed with invasive aspergillosis as shown in the table below.

Table 15

Sensitivity with Platelia™ *Aspergillus* Ag

Proven or Probable Invasive Aspergillosis in Lung Transplant Recipients By patient

Diagnosis	N	Index ≥ 0.5	Sensitivity	95% Confidence Interval
Proven Aspergillosis	2	1	1/2 (50.0%)	9.4 - 90.6%
Probable Aspergillosis	4	3	3/4 (75.0%)	30.0 - 95.4%
Combined Proven and Probable Aspergillosis	6	4	4/6 (66.7%)	30.0 - 90.3%

III. Hematologic disease patients with invasive aspergillosis

Sensitivity was also evaluated in a third study in 58 samples from 58 hematologic disease patients diagnosed with invasive aspergillosis as shown in the table below. In the study a retrospective analysis was performed on BAL samples from high risk hematology patients using the Platelia™ *Aspergillus* EIA. The data from this published study below was evaluated to establish the performance characteristics of the Platelia™ *Aspergillus* EIA on BAL fluid [29].

Table 16

Proven or Probable Invasive Aspergillosis in Hematologic Disease Patients

Diagnosis	N	Index ≥ 0.5	Sensitivity	95% Confidence Interval
Proven Aspergillosis	31	31	31/31 (100%)	89.0 - 100%
Probable Aspergillosis	27	26	26/27 (96.3%)	81.7 - 99.3%
Combined Proven and Probable Aspergillosis	58	57	57/58 (98.3%)	90.8 - 99.7%

B. Specificity

Specificity was evaluated in a total of 98 BAL samples from 57 SOT recipients and 305 BAL samples from 110 Lung Transplant recipients without invasive aspergillosis and is shown in the table below.

Results are presented by samples from transplant recipients with and without mold colonization:

Table 17

Specificity by Sample
Combined SOT and Lung Transplant Recipients without Invasive Aspergillosis
N = 403 BAL Fluids

Diagnosis	N	Index < 0.5	Negative (%)	95% Confidence Interval
Controls without colonization	341	330	330/341(96.8%)	94.3 - 98.2%
Controls with colonization	62	50	50/62 (80.6%)	69.1 - 88.6%
Control Total	403	380	380/403(94.3%)	91.6 - 96.2%

Specificity in BAL samples from the combined SOT and lung transplant recipients without Invasive Aspergillosis is presented by transplant type in the table 18 below:

Table 18

Specificity by Sample
Combined SOT and Lung Transplant Recipients without Invasive Aspergillosis By Transplant Type
N = 403 BAL Fluids

Transplant Type	N	Index < 0.5	Negative (%)	95% Confidence Interval
Heart	28	25	25/28 (89.3%)	72.8 - 96.3%
Kidney	25	22	22/25 (88.0%)	70.0 - 95.8%
Liver	23	22	22/23 (95.7%)	79.0 - 99.2%
Lung	327	311	311/327 (95.1%)	92.2 - 97.0%
Total	403	380	380/403 (94.3%)	91.6 - 96.2%

Specificity was also evaluated in a total of 41 BAL samples from 41 hematologic disease patients without invasive aspergillosis and is shown in the table below.

Table 19

Specificity by Sample

Hematologic Disease Patients without Invasive Aspergillosis

N= 41

Diagnosis	N	Index < 0.5	Negative (%)	95% Confidence Interval
Control Patients	41	33	33/41 (80.5%)	66.0 – 89.8%

16- BIBLIOGRAPHY

1. **Ansorg, R., R. Van Den Boom, and P.M. Rath. 1997**. Detection of *Aspergillus* galactomannan antigen in foods and antibiotics. Mycoses 40 : p. 353-7.
2. **Ascioglu, S., J. H. Rex, B. De Pauw, J. E. Bennett, J. Bille, F. Crokaert, D. W. Denning, J. P. Donnelly, J. E. Edwards, Z. Erjavec, D. Fiere, O. Lortholary, J. Maertens, J. F. Meis, T. F. Patterson, J. Ritter, D. Selleslag, P. M. Shah, D. A. Stevens and T. J. Walsh. 2002**. Defining opportunistic invasive fungal infections in immunocompromised patients with cancer and hematopoietic stem cell transplants: an international consensus. Clin.Infect.Dis. 34: p. 7-14.
3. **Aubry, A., R. Porcher. J. Bottero, S. Touratier, T. Leblanc, B. Brethon, P. Rousselot, E. Raffoux, J. Menotti, F. Derouin, P. Ribaud and A. Sulahian 2006**. Occurrence and Kinetics of False-Positive *Aspergillus* GalactomannanTest Results following Treatment with ß-Lactam Antibiotics in Patients with Hematological Disorders. J. Clin. Microbiol. 44: p. 389-394.
4. **Barnes P. D. and K. A. Marr. 2007** Risks, diagnosis and outcomes of invasive fungal infections in haemotopoeitic stem cell transplant recipients. Brit. Journ. Haemotol. 139: p. 519-531.
5. **Becker M. J., E. J. Lugtenburg. J. J. Cornelissen, C. V.D. Schee, H. C. Hoogsteden and S. D. Marie. 2003** Galactomannan detection in computerized tomography-based broncho-alveolar lavage fluid and serum in haemotological patients at risk for invasive pulmonary aspergillosis. Br. J. Haemotol. 121(3): p. 448-457.
6. **Blijevens, N. M., J. P. Donelly, J. F. Meis, P. E. Verweij, and B. E. De Pauw. 2002** *Aspergillus* galactomannan antigen levels in allogeneic haemotopoietic stem cell transplant receipients given total parenteral nutrition. Transpl. Infect. Dis. 4: p. 64-65.
7. **Chambon-Pautas, C.,J. M. Costa, M.T. Chaumette, C. Cordonnier, and S. Bretagne. 2001** Galactomannan and polymerase chain reaction for the diagnosis of primary digestive aspergillosis in a patient with acute myeloid leukaemia. J. Infect. 43: p. 213-214.
8. **Clancy C., R. A. Jaber, H. L. Leather, J. R. Wingard, B. Staley, J. L. Wheat, C. Cline, K. H. Rand, D. Schain, M. Baz and M. H. Nyugen. 2007** Bronchoalveolar Lavage Galactomannan in Diagnosis of Invasive Pulmonary Aspergillosis among Solid-Organ Transplant Recipients. J. Clin. Microbiol. 45(6): p. 1759-1765.
9. **De Repentigny, L., L. Kaufman, G. T. Cole, D. Kruse, J. P. Latge, and R. C. Matthews. 1994**. Immunodiagnosis of Invasive Fungal Infections. J Med Vet Mycol 32: p. 239-252.
10. **Denning, D. W. 1998**. Invasive Aspergillosis. Clin Infect.Dis. 26: p. 781-803.
11. **Desai R, L.A. Ross and J. A. Hoffman Poster AAA 2008**. The Role of Bronchoalveolar Lavage Galactomannan Assay in the Diagnosis of Invasive Aspergillosis in Pediatric Populations.
12. **Erjavec, Z. and P. E. Verweij. 2002**. Recent progress in the diagnosis of fungal infections in the immunocompromised host. Drug Resist. Updat. 5: p.3-10.
13. **Gangneux, J., D. Lavarde, S. Bretagne, C. Guiguen and V. Gandemer. 2002**. Transient *Aspergillus* antigenaemia: think of milk. Lancet. 359(9313):1251.
14. **Hage,C. A., J. M. Reynolds, M. Durkin, L. J. Wheat, K. S. Knox. 2007**. Plasmalyte as a Cause of false-positive results for *Aspergillus* galactomannan in bronchoalveolar lavage fluid. J. Clin. Microbiol. 45: p. 676-677.

15. **Herbrecht, R., V. Letscher-Bru, C. Oprea, B. Lioure, J. Waller, F. Campos, O. Villard, K. L. Liu, S. Natarajan-Ame, P. Lutz, P.Dufour, J. P. Bergerat, and E. Candolfi. 2002**. *Aspergillus* galactomannan detection in the diagnosis of Invasive Aspergillosis in cancer patients. J Clin. Oncol. 20: p.1898-1906.
16. **Herbrecht, R., D. Denning, T. Patterson, J. Bennett, R. Greene, J. Oestmann, W. Kern, K. Marr, P. Ribaud, O. Lortholary, R. Sylvester,R. Rubin, J. Wingard, P. Stark, C. Durand, D. Caillot, E. Thiel, P. Chandrasekar, M. Hodges, H. Schlamm, P. Troke, B. DePauw. 2002**. Voriconazole Versus Amphotericin B for Primary Therapy of Invasive Aspergillosis. N Engl J Med. 347, 6: p. 408-415.
17. **Hussain S., D.L. Paterson, S. M. Studer, M. Crespo, J. Pilewski, M. Durkin, J.L. Wheat, B. Johnson, L. Mclaughlin, C. Bentsen, K. McCurry and N. Singh. 2007** *Aspergillus* Galactomannan Antigen in the Bronchoalveolar Lavage Fluid for the Diagnosis of Invasive Aspergillosis in Lung Transplant Recipients. Transplantation 83(10): p. 1330-1336.
18. **Hussain S., C. J. Clancy, M.H. Nyugen, S. Swartzentruber, H. Leather, A. M. LeMonte, M.M. Durkin, K. S. Knox, C. A. Hage, C. Bentsen, N. Singh, J.R. Wingard and L.J. Wheat. 2008** Performance Characteristics of the Platelia™ *Aspergillus* AG for detection of *Aspergillus* galactomannan antigen in bronchoalveolar lavage fluid. Clin. Vaccine Immunol.15(12) : p. 1760-1763.
19. **Khan ZU, Ahmad S, and Theyyathel AM. 2008** Detection of *Aspergillus fumigatus*-specific DNA, (1-3)-beta-d-glucan and galactomannan in serum and bronchoalveolar lavage specimens of experimentally infected rats. Mycoses; 51: p. 129-35.
20. **Klont R.R., M.A.S.H. Mennink-Kersten and P. E. Verweij. 2004** Utility of *Aspergillus* Antigen Detection in Specimens Other than Serum Specimens. Clin. Infect. Diseas. 39: p. 1467-74.
21. **Knox KS, Rose AS, and Hage CA. 2007** Rapid Fungal Diagnosis: The Utility of Bronchoalveolar Lavage for Pneumocystis and Endemic Mycoses. Current Fungal Infection Reports; 1: p. 153-8.
22. **Kwak EJ and Nyugen MH. 2008** Galactomannan Detection in Bronchoalveolar Lavage Fluid. Current Fungal Infection Reports; 2: p.206-213.
23. **Latge, J. P. 1995**. Tools and trends in the detection of *Aspergillus fumigatus*. Curr Top Med Mycol 6: p. 245-281.
24. **Latge, J. P. 1999** *Aspergillus fumigatus* and Aspergillosis. Clin Microbiol Rev 12[2], 310-50.
25. **Latge, J. P., H. Kobayashi, J. P. Debeaupuis, M. Diaquin, J. Sarfati, J. M. Wieruszeski, E. Parra, J. P. Bouchara, and B. Fournet. 1994**. Chemical and immunological characterization of the extracellular galactomannan of *Aspergillus fumigatus*. Infect.Immun. 62: p. 5424-5433.
26. **Letscher-Bru, V., A. Cavalier, E. Pernot-Marino, H. Koenig, D. Eyer, J. Waller amd E. Candolfi. 1998**. Recherche d'antigene galactomannane aspergillaire circulant par Platelia™ *Aspergillus*: antigenemies positives persistantes en l'absence d'infection. J. Med. Mycol. 8:p. 112-113.
27. **Maertens, J., J. Verhaegen, H. Demuynck, P. Brock, G. Verhoef, P. Vandenberghe, J. Van Eldere, L. Verbist, and M. Boogaerts. 1999**. 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. 37: p. 3223-3228.
28. **Maertens, J., J. Verhaegen, K. Lagrou, J. Van Eldere, and M. Boogaerts. 2001**. 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 97: p. 1604-1610.
29. **Maertens J., V. Maertens, K. Theunissen, W. Meersseman, P. Meersseman, S. Meers, E. Verbeken, G. Verhoef, J. V. Eldere and K. Lagrou. 2009.** Bronchoalveolar Lavage Fluid Galactomannan for the Diagnosis of Invasive Pulmonary Aspergillosis in Patients with Hematologic Diseases. Clin. Infec. Diseas. 49: 1688-93.
30. **Marr K. A., S. A. Balajee, L. McLaughlin, M. Tabouret, C. Bentsen and T.J. Walsh**. 2004. Detection of Galactomannan Antigenemia by Enzyme Immunoassay for the Diagnosis of Invasive Aspergillosis: Variables That Affect Performance. J. Infect. Dis. 190 :641-9
31. **Marr K. A., M. Laverdiere, A. Gugel and W. Leisenring. 2005**. Antifungal therapy decreases sensitivity of the *Aspergillus* galactomannan enzyme immunoassay. Clin. Infect. Dis 40: p. 1762-9.
32. **Mattei, D., D. Rapezzi, N. Mordini, F.Cuda, C. Lo Nigro, M. Musso, A. Arnelli, S. Cagnassi, and A. Gallamini. 2004**. False-positive *Aspergillus* galactomannan enzyme-linked immunosorbent assay results in vivo during amoxicillin-clavulanic acid treatment. J. Clin. Microbiol. 42: p. 5362-5363.

33. **Mennink-Kersten M. A. S. H., D. Ruegebrink, R. Klont, A. Warris, H. J. M. Op den Camp and P. Verweij. 2005** Bifidobacterial Lipoglycan as a New Cause for False-Positive Platelia™ *Aspergillus* Enzyme Immunoabsorbent Assay Reactivity. J. Clin. Microbiol. 43(8): 3925-3931.
34. **Meersseman W., K. Lagrou, J. Maertens, A. Wilmer, G. Hermans, S. Vanderschueren, I. Spriet, E. Verbeken and E. V. Wijngaerden. 2008** *galactomannan* in Bronchoalveolar Lavage Fluid. Am. J. Respi. Crit. Care Med 177: p. 27-34.
35. **Musher B., D. Fredericks, W. Leisenring, S. A. Balajee, C. Smith and K. Marr. 2004** *Aspergillus galactomannan* Enzyme Immunoassay and Quantitative PCR for Diagnosis of Invasive Aspergillosis with Bronchoalveolar Lavage Fluid. J. Clin. Microbiol. 42(12): p. 5517-5522.
36. **Nareddy, S., P. H. Chandrasekar. 2008**. False-positive *Aspergillus galactomannan* (GM) assay in histoplasmosis. J. Infection 56: p. 80-81.
37. **Nguyen MH, R. Jaber, H.L. Leather, J. R. Wingard, B. Staley, L. J. Wheat, C. L. Cline, M. Baz, K.H. Rand and C. J. Clancy. 2007** Use of bronchoalveolar lavage to detect *galactomannan* for diagnosis of pulmonary aspergillosis among nonimmunocompromised hosts. J Clin Microbiol; 45:2787-92.
38. **Patterson D. L. and N. Singh. 1999**. Invasive Aspergillosis in Transplant Recipients. Medicine. 78(2) : p. 123-38.
39. **Pauw B.D., Walsh T. J., Donelly J. P., Stevens D.A., Edwards J. E., Calandra T., Pappas P. G., Maertens J., Lortholary O., Kauffman C. A., Denning D.W., Patterson T.F., Maschmeyer G., Bille J., Dismukes W.E., Herbrecht R., Hope W. W., Kibbler C.C., Kulberg B. J., Marr K. A., Munoz P., Odds F. C., Perfect J. R., Restrepo A., Ruhnke M., Segal M., Segal B. H., Sobel J. D., Sorell T.C., Viscoli C., Wingard J.R., Zaoutis T. and J.E. Bennett. 2008**
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 Consensu Group. Clin. Infectious Disease 46, p. 1813-1821.
40. **Penack O., P. Rempf, B. Graf, I. W. Blau and E. Thiel. 2008** *Aspergillus galactomannan* testing in patients with long-term neutropenia: implications for clinical management. Ann Oncol. 19(5): p. 984-9, Epub 2008.
41. **Racil, Z., I. Kocmanova, M. Lengerova, J. Winterova, J. Mayer. 2007**. Intravenous PLASMA-LYTE as a Major Cause of False-Positive Results of Platelia™ *Aspergillus* Test for *galactomannan* Detection in Serum. J. Clin. Microbiol. 45(2): p. 3141-3142.
42. **Salonen J., O-P. Lehtonen, M-R Terasjarvi and J. Nikoskelainen. 2000**. *Aspergillus* Antigen in Serum, Urine and Bronchoalveolar Lavage Specimens of Neutropenic Patients in Relation to Clinical Outcome. Scand J. Infec. Dis. 32: p.485-490.
43. **Sanguinetti M., B. Posteraro, L. Pagano, G. Pagliari, L. Fianchi, L. Mele, M. L. Sorda, A. Franco and G. Fadda. 2003**. 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. 41(8): p.3922-3925.
44. **Siemann M., M. Koch-Dorfler and M. Gaude 1998**. False-positive results in premature infants with the Platelia™ *Aspergillus* sandwich enzyme-linked immunoabsorbent assay. Mycoses. 41(9-10): 373-7.
45. **Stynen, D., A. Goris, J. Sarfati, and J. P. Latge. 1995**. A new sensitive sandwich enzyme-linked immunosorbent assay to detect galactofuran in patients with Invasive Aspergillosis. J.Clin. Microbiol. 33: p. 497-500.
46. **Stynen, D., J. Sarfati, A. Goris, M. C. Prevost, M. Lesourd, H. Kamphuis, V. Darras, and J. P. Latge. 1992**. Rat monoclonal antibodies against *Aspergillus galactomannan*. Infect.Immun. 60: p. 2237-2245.
47. **Sulahian, A., F. Boutboul, P. Ribaud, T. Leblanc, C. Lacroix, and F. Derouin. 2001**. 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 91: p. 311-318.

48. **Sulahian, A., M. Tabouret, P. Ribaud, J. Sarfati, E. Gluckman, J. P. Latge, and F. Derouin. 1996**. Comparison of an enzyme immunoassay and latex agglutination test for detection of *galactomannan* in the diagnosis of Invasive Aspergillosis. Eur.J Clin. Microbiol. Infect. Dis. 15: p. 139145.
49. **Surmont ,I., W. Stockman. 2007**. Gluconate-containing intravenous solutions: Another cause of false-positive *galactomannan* assay reactivity. J. Clin. Microbiol. 45: p. 1373.
50. **Swanink, C. M., J. F. Meis, A. J. Rijs, J. P. Donnelly, and P. E. Verweij. 1997**. Specificity of a sandwich enzyme-linked immunosorbent assay for detecting *Aspergillus galactomannan*. J Clin. Microbiol. 35: p. 257-260.
51. **Upton A., A. Gugel, W. Leisenring, A. Limaye, B. Alexander, R. Hayden and K. Marr. 2005**. Reproducibility of Low *galactomannan* Enzyme Immunoassay Index Values Tested in Multiple Laboratories. J. Clin. Microbiol, 43: p 4796-4800.
52. **Verdaguer V., T. J. Walsh, W. Hope and K. Cortez. 2007** *galactomannan* antigen detection in the diagnosis of invasive aspergillosis. Expert Rev. Mol. Diagn. 7(1):p. 21-32.
53. **Verweij, P. E., E. C. Dompeling, J. P. Donnelly, A. V. Schattenberg, and J. F. Meis. 1997**. Serial monitoring of *Aspergillus* antigen in the early diagnosis of Invasive Aspergillosis. Preliminary investigations with two examples. Infection 25: p. 86-89.
54. **Verweij, P. E. and J. F. Meis. 2000**. Microbiological diagnosis of Invasive Fungal Infections in transplant recipients. Transpl.Infect.Dis. 2: p. 80-87.
55. **Verweij, P. E., D. Stynen, A. J. Rijs, B. E. de Pauw, J. A. Hoogkamp -Korstanje, and J. F. Meis. 1995**. Sandwich enzyme-linked immunosorbent assay compared with Pastorex latex agglutination test for diagnosing Invasive Aspergillosis in immunocompromised patients. J. Clin. Microbiol. 33: p. 1912-1914.
56. **Verweij, P. E., C. M. Weemaes, J. H. Curfs, S. Bretagne, J. F. Meis. 2000**. Failure to detect circulating *Aspergillus* markers in a patient with chronic granulomatous disease and Invasive Aspergillosis. J Clin. Microbiol. 38: p. 3900-3901.
57. **Verweij P., J-P Latge, A. J. J. M. Rijs, W. J. G. Melchers, B. E. D. Pauw, J. A. A. Hoogkamp-Korstanje. 1995** Comparison of Antigen Detection and PCR Assay Using Bronchoalvealor Lavage Fluid for Diagnosing Invasive Pulmonary Aspergillosis in Patients Receiving Treatment for Hematological Malignancies. J. Clin. Microbiol. 33(12): p. 3150-3153.
58. **Walsh T. J., R.L. Schaufele, T. Sein, J. Gea-Banacloche, M. Bishop, N. Young, R. Childs, J. Barrett, H. L. Malech, and S.M. Holland. 2002**. Reduced expression of *galactomannan* antigenemia in patients with Invasive Aspergillosis and chronic granulomatous disease or Job's syndrome. Abstracts of the 40th Annual Meeting of the Infectious Diseases Society of America. Arlington, VA. P. 105 ; Abstr. 345.
59. **Wheat, L. J., E. Hackett, M. Durkin, P. Connolly, R. Petraitiene, T. J. Walsh, K. Knox, C. Hage. 2007**. Histoplasmosis-associated cross-reactivity in the Bio-Rad Platelia™ *Aspergillus* enzyme immunoassay. Clin. Vaccine Immunol. 14 (5): p. 638-40.
60. **Wheat J.L., A. M. Monte, M.M. Durkin, S.L. Swartzentruber, K.K. Knox, C.A. Hage, C. Bentsen, S. Husain, N. Singh, C.J. Clancy, M.H. Nyugen AAA 2008**. Poster Detection of *Aspergillus galactomannan* in BAL in the Platelia Aspergilllus AG, as performed at MiraVista Diagnostics. http://www.miravistalabs.com Site verified June 9, 2008.
61. **Wheat J. and T.J. Walsh. 2008** Diagnosis of Invasive Aspergillosis by *galactomannan* Antigenemia Detection using an enzyme immunoassay. Eur J Clin Microbiol Infect Dis; 27:245-51.
62. **Yeo, S. F. and B. Wong. 2002**. Current Status of Nonculture Methods for Diagnosis of Invasive Fungal Infections. Clin.Microbiol.Rev. 15: p. 465-484.

(BG) • Този продукт съдържа човешки или животински компоненти. Бъдете внимателни при работа с него.
(CZ) • Tento výrobek obsahuje lidské nebo zvířecí komponenty. Zacházejte s ním opatrně.
(DE) • Dieses Produkt enthält Bestandteile menschlichen oder tierischen Ursprungs. Vorsichtig handhaben.
(DK) • Dette produkt indeholder humane og animalske komponenter. Skal behandles med forsigtighed.
(EE) • Käesolev toode sisaldab inim-või loomseid komponente. Käsitseda ettevaatlikult.
(EN) • This product contains human or animal components. Handle with care.
(ES) • Este producto contiene componentes humanos o animales. Manejar con cuidado.
(FI) • Tässä tuotteessa on ihmisestä tai eläimistä peräisin olevia osia. Käsittele varovasti.
(FR) • Ce produit contient des composants d'origine humaine ou animale. Manipuler avec précaution.
(GR) • Αυτό το προϊόν περιέχει ανθρώπινα ή ζωικά στοιχεία. Χειριστείτε το με προσοχή.
(HR) • Ovaj proizvod sadrži ljudske ili životinjske sastojke. Pažljivo rukovati.
(HU) • A készítmény emberi vagy állati eredetű összetevőket tartalmaz. Óvatosan kezelendő.
(IT) • Questo prodotto contiene componenti umane o animali. Maneggiare con cura.
(LT) • Šiame produkte yra žmogiškosios arba gyvūninės kilmės sudėtinių dalių. Elgtis atsargiai.
(MT) • Dan il-prodott fih komponenti umani jew tal-annimali. Uża b'attenzjoni.
(NL) • Dit product bevat menselijke of dierlijke bestanddelen. Breekbaar.
(NO) • Dette produktet inneholder humane eller animalske komponenter. Håndteres med forsiktighet.
(PL) • Niniejszy produkt zawiera składniki pochodzenia ludzkiego lub zwierzęcego. Należy obchodzić się z nim ostrożnie.
(PT) • Este medicamento contém componentes de origem humana ou animal. Manuseie com cuidado.
(RO) • Acest produs conține materiale de origine umană sau animală. Manevrați-l cu grijă.
(SE) • Denna produkt innehåller beståndsdelar från människa eller djur. Hantera produkten varsamt.
(SI) • Izdelek vsebuje človeške ali živalske sestavine. Rokujte previdno.
(SK) • Tento výrobok obsahuje ľudské alebo zvieracie zložky. Narábajte s ním opatrne.

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

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

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

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

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

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

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

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

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

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

(GR)
Κίνδυνος
Προκαλεί σοβαρά δερματικά εγκαύματα και οφθαλμικές βλάβες. Μπορεί να προκαλέσει αλλεργική δερματική αντίδραση.
Να φοράτε προστατευτικά γάντια/προστατευτικά ενδύματα/μέσα ατομικής προστασίας για τα μάτια/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/Επισκεφθείτε γιατρό. 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.
Nositi zaštitne rukavice/zaštitnu odjeću/zaštitu za oči/zaštitu za lice. U SLUČAJU DODIRA S OČIMA: oprezno ispirati vodom nekoliko minuta. Ukloniti kontaktne leće ukoliko ih nosite i ako se one lako uklanjaju. Nastaviti ispiranje. AKO SE PROGUTA: isprati usta. NE izazivati povraćanje. U SLUČAJU DODIRA S KOŽOM (ili kosom): odmah ukloniti/skinuti svu zaganenu odjeću. Isprati kožu vodom/tuširanjem. U slučaju nadražaja ili osipa na koži: zatražiti savjet/pomoć liječnika. Odložite sadržaje /spremnike u skladu s lokalnim/regionalnim/nacionalni/međunarodnim odredbama.

(HU)

Veszély

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

(IT)

Pericolo

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

(LT)

Pavojinga

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

(NL)

Gevaar

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

(NO)

Fare

Forársaker alvorlige hudforbrenninger og øyeskader. Kan forårsake allergiske hudreaksjoner.
Bruk vernehansker/verneklær/vernebriller/ansiktsskjerm. VED KONTAKT MED ØYNENE: Skyll forsiktig med vann i opptil flere minutter. Fjern evt. kontaktlinser såfremt dette er lett mulig. Fortsett skyllingen. VED SVELGING: Skyll munnen. IKKE fremkall brekninger. VED HUDKONTAKT (eller kontakt med hår): Alle tilsølte klær må fjernes straks. Vask/dusj huden med vann. Ved hudirritasjon eller -utslett: Kontakt / tilkall lege. Innholdet / emballasjen skal avhendes i henhold til de lokale / regionale / nasjonale / internasjonale forskrifter.

(PL)

Niebezpieczeństwo

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

(PT)

Perigo

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

(RO)

Pericol

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

(SE)

Fara

Orsakar allvarliga frätskador på hud och ögon. Kan orsaka allergisk hudreaktion.
Använd skyddshandskar/skyddskläder/ögonskydd/ansiktsskydd. VID KONTAKT MED ÖGONEN: Skölj försiktigt med vatten i flera minuter. Ta ur eventuella kontaktlinser

om det går lätt. Fortsätt att skölja. VID FÖRTÄRING: Skölj munnen. Framkalla INTE kräkning. VID HUDKONTAKT (även håret): Ta omedelbart av alla nedstänkta kläder. Skölj huden med vatten/duscha. Vid hudirritation eller utslag: Sök läkarhjälp. Innehållet / behållaren avfallshanteras enligt lokala / regionala / nationella / internationella föreskrifter.

(SI)

Nevarno

Povzroča hude opekline kože in poškodbe oči. Lahko povzroči alergijski odziv kože.
Nositi zaščitne rokavice/zaščitno obleko/zaščito za oči/zaščito za obraz. PRI STIKU Z OČMI: previdno izpirajte z vodo nekaj minut. Odstranite kontaktne leče, če jih imate in če to lahko storite brez težav. Nadaljujte z izpiranjem. PRI 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. Vsebino/vsebnik odstranite v skladu z lokalnimi/regionalnimi/narodnimi/mednarodnimi predpisi.

(SK)

Nebezpečenstvo

Provocačí arsuri grave ale pielii şi lezarea ochilor. Môže vyvolať alergickú kožnú reakciu.
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. Zneškodnenie obsahu/obalu v súlade s miestnymi/oblastnými/národnými/medzinárodnými nariadeniami.

NOTES

Distributed in the U.S. by:
Bio-Rad Laboratories
6565 185th Avenue NE
Redmond, WA 98052

Bio-Rad
3, boulevard Raymond Poincaré
92430 Marnes-la-Coquette France
Tel. : +33 (0) 1 47 95 60 00
Fax.: +33 (0) 1 47 41 91 33
www.bio-rad.com

2013/10
881115

For Customer Orders and Technical Service Call: 1-800-2-BIO-RAD (1-800-224-6723)