PLATELIA™ *Aspergillus* IgG

1 plate - Σ 96 REF 62783

DETECTION OF IgG ANTI-*ASPERGILLUS* ANTIBODIES IN HUMAN SERUM OR PLASMA USING AN IMMUNOENZYMATIC METHOD

IVD CE

881123 - 2013/11

BIO-RAD

Table of Content

1- INTENDED USE

Platelia™ *Aspergillus* IgG is an indirect microplate immunoenzymatic technique to detect IgG anti-*Aspergillus* antibodies in human serum or plasma.

2- INDICATIONS FOR USE

Platelia™ *Aspergillus* IgG is an assay that – when interpreted on the basis of the patient's clinical and therapeutic context and when carried out along with other diagnostic techniques such as radiological, cytological, immunological and mycological examinations – may be used as an aid in diagnosing *Aspergillus* pathologies.

3- CLINICAL INTEREST

Various chronic *Aspergillus* pathologies may be found in immuno-competent subjects, and their diagnosis often proves difficult.

A process of mould sensitization is at the root of allergic manifestations such as asthma, allergic broncho-pulmonary aspergillosis (ABPA), which represents the most exacerbated clinical form [4, 8]. Patients afflicted with mucoviscidosis constitute a population exposed to the risk of ABPA and are regularly monitored for this diagnosis [1, 2].

In subjects exposed to massive inhalation of spores, extrinsic alveolitis may be encountered; the best known forms are bird-raiser's disease and farmer's lung disease.

Aspergilloma represents the most typical non-allergenic chronic pathology that is the result of colonization of a pre-existent pulmonary cavity (tuberculosis, emphysema, sarcoidosis, lung cancer) by fungal mycelia forming an "*Aspergillus* ball" [4, 6, 10].

In the context of the other non-allergenic pathologies, chronic necrotic aspergillosis represents a particularly serious progressive mortal form.

In these various clinical manifestations, whether allergic or non-allergic, diagnosing aspergillosis is often difficult. This is because the clinical signs may suggest other mycosic, bacterial, viral, even cancerous affections. Radiological examination, which is characteristic for aspergilloma, is clearly less so for the other forms of aspergillosis where clinical and radiological examination only represent elements in a diagnostic orientation.

Biological parameters and, in particular, serological tests are indispensible to support this diagnosis [5]. Consequently, in aspergilloma risk patients, a serious but often clinically silent infection, serological monitoring proves to be relevant. Certain diagnosis of ABPA relies on five criteria including serological detection of the anti-*Aspergillus* antibody [13].

Platelia™ *Aspergillus* IgG, which is an assay used to detect class G immunoglobulins directed against a recombinant purified antigen of *Aspergillus*, represents a tool for diagnostic assistance of these chronic forms of aspergillosis that are observed in immunocompetent subjects [3].

In addition, the presence of anti-*Aspergillus* antibodies has recently been described in onco-hematological patients before instituting an immuno-suppressant treatment for bone marrow graft. These studies suggest detection of an *Aspergillus* colonization when the patient is admitted to hospital or in the balance prior to the graft in these patients who will become a risk population for invasive aspergillosis after immunosuppressant treatments are initiated.

4- PRINCIPLE OF THE PROCEDURE

Platelia™ *Aspergillus* IgG is a 2-phase indirect microplate immuno-enzymatic technique used to detect IgG anti-*Aspergillus* antibodies in human serum or plasma.

Samples of diluted serum or plasma are distributed in the wells of the microplate sensitized with purified recombinant *Aspergillus* antigen [7].

After incubation at 37°C, the strips are washed to remove any free material.

The conjugate (mouse anti-human IgG monoclonal antibody marked with peroxidase) is added to each well on the microplate and incubated at 37°C.

A complex is formed if IgG anti-*Aspergillus* is present in the human sample: Ag *Aspergillus* - human IgG anti-*Aspergillus* - mouse anti-human IgG Ab/ peroxidase.

The strips are washed to remove any free material.

Addition of chromogen containing peroxidase substrate and incubation at room temperature is used to reveal any complexes that may have been formed.

The enzymatic reaction is stopped by adding 1N sulfuric acid.

A spectrophotometer set to 450/620 nm is used to read the optical density.

5- REAGENTS

Reagents are provided in sufficient quantity to carry out 96 determinations or a maximum of 9 test runs.

For storage conditions and expiry date of the reagents refer to the indications on the box.

Let all reagents reach room temperature (+18-30°C) before using them. Return all reagents to +2-8°C immediately after using them. Return the unused strips to the original pouch and seal with care. Do not remove the desiccant.

Component		Contents	Quantity
R1	**Microplate**	**Microplate:** - 96 wells (12 strips each containing 8 wells) sensitized with the purified recombinant *Aspergillus* antigen.	1
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	**Calibrator 0**	**Calibrator 0 AU/ml (ready to use):** - Tris-NaCl buffer that does not contain IgG anti-*Aspergillus* - Preservative: 0.15% ProClin™ 300	1 x 2.5 ml
R4a	**Calibrator 10**	**Calibrator 10 AU/ml (ready to use):** - Human serum containing anti-*Aspergillus* antibodies - Preservative: 0.15% ProClin™ 300	1 x 2.5 ml
R4b	**Calibrator 20**	**Calibrator 20 AU/ml (ready to use):** - Human serum containing anti-*Aspergillus* antibodies - Preservative: 0.15% ProClin™ 300	1 x 2.5 ml
R4c	**Calibrator 40**	**Calibrator 40 AU/ml (ready to use):** - Human serum containing anti-*Aspergillus* antibodies - Preservative: 0.15% ProClin™ 300	1 x 2.5 ml
R4d	**Calibrator 80**	**Calibrator 80 AU/ml (ready to use):** - Human serum containing anti-*Aspergillus* antibodies - Preservative: 0.15% ProClin™ 300	1 x 2.5 ml
R6	**Conjugate**	**Conjugate (ready to use)** - Mouse anti-human IgG monoclonal antibody marked with peroxidase - Phenol red - Preservative: 0.3% ProClin™ 300	1 x 26 ml
R7a	**Sample Diluent 1**	**Sample diluent solution 1 (ready to use):** - Tris-NaCl buffer, - 0.1% Tween® 20, - Phenol red, - Preservative: 0.151% ProClin™ 300	1 x 28 ml

Component		Contents	Quantity
R7b	**Sample Diluent 2**	**Sample diluent solution 2 (ready to use):** - Tris-NaCl buffer, - 0.1% Tween® 20, - Bromocresol purple, - Preservative: 0.151% ProClin™ 300	1 x 26 ml
R9	**Chromogen TMB**	**Chromogen TMB solution (ready to use)** - 3,3',5,5'-tetramethylbenzidine (< 0.1%) solution, H_2O_2 (<1.0%)	1 x 28 ml
R10	**Stopping Solution**	**Stopping solution (ready to use):** - 1N sulfuric acid solution	1 x 28 ml

6- HEALTH AND SAFETY INSTRUCTIONS

1. For *in vitro* diagnostic only.
2. For professional use only.
3. Use of this assay with samples other than human serum or plasma is not advisable.
4. Calibrators R4a, R4b, R4c and R4d are prepared from human serum that tested negative for anti-HIV-1, anti-HIV-2, anti-HCV antibodies as well as with HBs antibodies using CE marked tests. However, all reagents must be handled as if they were potentially infectious. All tests must be carried out in compliance with the OSHA standard relating to pathogenic agents transmitted hematogenously, bio-safety level 2 or in compliance with other adapted bio-safety practices.
5. Wear protective clothing including a laboratory coat, eye and face protection and disposable gloves (gloves made out of synthetic material without latex are recommended) and handle kit reagents as well as patient samples according to the required Good Laboratory Practices (GPL). Wash hands carefully after performing the assay.
6. Do not pipette orally.
7. Do not smoke, drink or eat in areas where samples or kit reagents are handled.
8. Avoid splashing samples or solutions.
9. Surfaces stained with a contaminating liquid that does not contain acid must be carefully cleaned using an effective disinfectant. Disinfectants that can be used are (but are not limited to) a solution of Javel water diluted to 10% (0.5% solution of sodium hypochlorite), 70% ethanol or 0.5% Wescodyne Plus™. The material used in cleaning must be disposed of in a special container for contaminated waste products.

CAUTION: Never put solutions containing Javel water in the steam sterilizer.

10. If the contaminating liquid is an acid, stained surfaces must be wiped or neutralized using sodium bicarbonate and the area must be rinsed and dried; in the event that the contaminating liquid contained biologically hazardous material, wash the area with a chemical disinfectant.
11. Eliminate all samples and reagents used for the assay as if they were potentially infectious. Hazardous chemical and biological waste products must be eliminated in compliance with the requirements in force.
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. THE FROZEN SAMPLES, STORED UNDER CONDITIONS UNKNOWN TO US MAY YIELD FALSE POSITIVE RESULTS DUE TO FUNGAL AND/OR BACTERIAL CONTAMINATION.
2. Do not use the kit or one of the reagents in the kit after expiry date.
3. Do not mix or combine reagents from cases with different batch numbers during the same series.

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

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

**** on the vial label***

4. Before dispensing, wait 30 minutes for the reagents to reach room temperature (+18 to +30°C).

5. Preferably utilize single use equipment. If this is not possible, use glass containers that have been thoroughly washed and rinsed with distilled water.
6. Check whether pipettes are exact and whether the instruments used are working properly.
7. Carefully reconstitute reagent R2, taking care to avoid any contamination.
8. The enzymatic reaction is highly sensitive to any metals or metallic ions. Consequently, no metal item should be in contact with the various solutions containing the conjugate or the substrate solution.
9. When pipetting calibrators and samples, use a new pipette tip for each well to avoid any contamination.
10. To ensure that wells are washed adequately, carry out the recommended number of washing cycles and make sure that all wells are completely filled and then completely emptied. Washing should be carried out using a microplate washer.
11. Do not let the microplate dry out between the end of the washing cycle and adding reagents.
12. Do not use the same bottle for the conjugate and the development solution.
13. Avoid exposing the chromogen solution or the revelation solution to strong light during storage or incubation. Do not allow solutions containing chromogen to come into contact with an oxidizing agent.
14. The Chromogen (R9) should be colourless. Appearance of blue colouring indicates that the reagent is unusable and should be replaced.
15. Avoid the stopping solution coming into contact with any oxidizing agent, metal or metallic ions.
16. Do not pour surplus undistributed conjugate back into the original vial.

8- REAGENT PREPARATION AND STORAGE

Microplate (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. Close the pouch carefully and put it in a location 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 the washing solution by diluting the concentrated solution 20 times in distilled water: 50 ml of R2 in 950 ml of distilled water. (Provide 650 ml of diluted washing solution for an entire plate of 12 strips excluding the dead volume of used washer). After dilution, the washing solution can be stored for 14 days at +2-30°C.

After the concentrated washing solution stored at +2-30°C is opened, it is stable until the expiry date shown on the label if there is no contamination.

Calibrator 0 (R3), calibrator 10 (R4a), calibrator 20 (R4b), calibrator 40 (R4c), calibrator 80 (R4d):

The calibrators are ready to use.

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

Conjugate (R6), Sample diluent 1 (R7a), Sample diluent 2 (R7b), TMB chromogen 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 Solution (R10):

This reagent is ready to use.

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.

9- SAMPLES

1. The tests are carried out on samples of serum or plasma taken on EDTA, sodium heparin or sodium citrate anti-coagulant.
2. Comply with the following guidelines for sampling, processing and storing these blood samples:
   - Take a blood sample according to the practices in use.
   - For serum, let the clot form completely before centrifuging.
   - Keep the tubes closed.
   - After centrifugation, extract the serum or the plasma and store it in a closed tube.
   - Samples are stored at +2-8°C if the assay is carried out within 4 days.
   - If the assay is not carried out within 4 days, samples are frozen at -20°C (or -80°C).
   - You should not perform more than five freezing/thawing cycles. The samples must be carefully homogenized (Vortex) after thawing and before the assay is carried out.

3. Results are not affected by samples containing 90 g/l of albumin or 100 mg/l of unconjugated bilirubin, lipemic samples containing the equivalent of 36 g/l of triolein (triglyceride) or hemolyzed samples containing 10 g/l of hemoglobin.
4. Do not heat the samples.

10- PROCEDURE

Equipment provided

See the REAGENTS chapter

Equipment that is required but not provided

1. Sterile distilled or demineralized water to dilute the concentrated washing solution.
2. Absorbent paper.
3. Single use gloves.
4. Protective goggles.
5. Sodium hypochlorite (Javel water) and sodium bicarbonate.
6. Pipettes or multipipettes, whether automatic or semi-automatic, adjustable or set, that can measure and deliver 10 µl to 1000 µl, 1 ml, 2 ml and 10 ml.
7. 25 ml, 50 ml, 100 ml and 1000 ml graduated test tubes.
8. Single use tubes
9. Contaminated waste container.
10. “Vortex” agitator.
11. Microplate incubator that can be set at 37°C ± 1°C (*).
12. Semi-automatic or automatic microplate washer (*).
13. Microplate reader equipped with 450 and 620 nm filters (*).

(*) Ask us for specific information on devices validated by our technical department.

EIA procedure

Comply with the stated protocol.

Comply with Good Laboratory Practices:

- Let the reagents reach room temperature (18-30°C) for at least 30 minutes before using them.
- Use all the calibrators every time the dosage is used to validate the assay.

Proceed as follows:

1. Carefully set up the plan for distributing and identifying calibrators and patient samples.

2. Pre-dilute the samples to be tested beforehand: at 1/20, i.e. 10 µl of serum or plasma + 190 µl of sample diluent 1 (R7a). Pre-diluting the sample results in a red colouring.
3. Take the frame and the strips (R1) out of their protective wrapping. Put the unused strips in their wrapping and seal it.
4. Distribute **190 µl** of sample diluent 2 (R7b) in the wells intended to hold the samples to be tested and add **10 µl** of pre-diluted samples at 1/20, gently mixing by suction repeated 2 or 3 times.

NB: At this stage of the procedure, distribution can be checked because after adding 10 µl of pre-diluted samples, the wells containing samples turn gray in colour. A cup that does not contain any sample is blue-violet in color.

5. Distribute the ready to use calibrators by 200 µl per well according to the following plan:
   - A1: Calibrator 0 (R3)
   - B1: Calibrator 10 AU/ml (R4a)
   - C1: Calibrator 20 AU/ml (R4b)
   - D1: Calibrator 40 AU/ml (R4c)
   - E1: Calibrator 80 AU/ml (R4d)

	1	2	3	4	5	6	7	8	9	10	11	12
A	R3	S4	S12									
B	R4a	S5										
C	R4b	S6										
D	R4c	S7										
E	R4d	S8										
F	S1	S9										
G	S2	S10										
H	S3	S11										

6. Cover the microplate with an **adhesive film**, pressing down over the entire surface area to ensure tightness.
7. Incubate the microplate in a dry microplate incubator **immediately** for 60 ± 5 minutes at 37°C (± 1°C).
8. Prepare the diluted washing solution (refer to chapter 8).
9. Remove the adhesive film. Aspirate the contents of each well into a container (containing sodium hypochlorite) for contaminated waste products.

10. Wash the microplate **4 times using a microplate washer** (with 800 µl of diluted washing solution). After the last wash, turn the microplate over and tap onto absorbent paper lightly to remove any remaining liquid.
11. Homogenize the contents of vial R6 by turning it upside down before using it. If you are using a multichannel pipette, only take the volume needed to carry out the series: provide 3.5 ml for two strips of 8 cups.
12. Distribute **200 µl** of R6 conjugate in each well.
13. Cover the microplate with an **adhesive film**, pressing down over the entire surface area to ensure tightness.
14. Incubate the microplate in a dry microplate incubator for 60 ± 5 minutes at 37°C (± 1°C).
15. Remove the adhesive film. Aspirate the contents of each well into a container (containing sodium hypochlorite) for contaminated waste products.
16. Wash the microplate 4 times **using a microplate washer** (with 800 µl of diluted washing solution). After the last wash, turn the microplate over and tap onto the absorbent paper lightly to remove any remaining liquid.
17. Away from bright light, **quickly** distribute 200 µl of the TMB (R9) chromogen solution in each well.
18. Incubate the microplate in darkness at room temperature (+18-30°C) for 30 ± 5 minutes. **Do not use adhesive film during this incubation stage**.
19. Add 100 µl of stopping solution (R10) to each well using the same sequence and rhythm as for adding the substrate solution. Mix well.
20. Carefully wipe the bottom of each microplate.
21. Read the optical density of each well at 450 nm (reference filter at 620 nm) within 30 minutes of adding the stopping solution (the strips must always be stored out of direct light before being read).
22. Check concordance between the reader printout and the microplate distribution plan before transcribing the results.

11- QUALITY CONTROL (VALIDITY CRITERIA)

Use the calibrators on each microplate every time the test is performed. The following criteria must be complied with to validate the assay:

• ***Optical density value:***
OD R4a > 0.200

• ***Ratios:***
OD R4a / OD R3 > 3.00
OD R4b / OD R4a > 1.20
OD R4c / OD R4b > 1.20
OD R4d / OD R4c > 1.00

12- INTERPRETATION OF RESULTS

Plotting the calibration curve

The calibration curve is defined using the 5 range points (calibrators) 0, 10, 20, 40 and 80 AU/ml.

Draw the calibration curve [OD = function (AU/ml)] by recording OD for calibrators R3, R4a, R4b, R4c and R4d on the vertical axis (Y axis) and then recording their respective concentrations in AU/ml on the horizontal axis (X axis). Opt for a point to point path linking the various range points.

Determining the concentration of IgG anti-Aspergillus antibodies (AU/ml) of the tested samples

The concentration in IgG anti-*Aspergillus* antibodies expressed in AU/ml can be determined for each sample tested from the curve plot in Section 12.

Interpretation of results

- Samples with concentrations less than 5 AU/ml **(C < 5)** are considered to be **«negative» for the presence of IgG** anti-*Aspergillus* antibody.
- Samples with concentrations between 5 and 10 AU/ml **(5 ≤ C < 10)** are considered to be **«intermediate» for the presence of IgG** anti-*Aspergillus* antibody.
- Samples with concentrations more than or equal to 10 AU/ml **(C ≥ 10)** are considered to be **«positive» for the presence of IgG** anti-*Aspergillus* antibody.

Range points used to draw the calibration curve cannot be used to obtain a precise titration of concentrations greater than 80 AU/ml.

If you want to determine the titer of highly positive samples more precisely, you should begin the assay again, carrying out an extra pre-dilution of the sample by diluting R7a:

- For sample with a titer **> 80 AU/ml** and with a **OD < 3.000**: first pre-dilute to 1/5 of the sample in R7a.
- For samples with a titer **> 80 AU/ml** and with a **OD ≥ 3.000**: first pre-dilute to 1/60 of the sample in R7a.

After this initial pre-dilution, follow the procedure stated in chapter 10 (pre-diluting to 1/20 in R7a and then diluting to 1/20 in R7b).

The titer of the highly positive sample will be calculated by multiplying the titer obtained by the factor of the first pre-dilution (i.e.: 5 or 60 according to the pre-dilution carried out).

An “intermediate” result can be confirmed by another sample taken from the patient within 2-3 weeks of the date of the sample that gave an intermediate titer.

In serological monitoring of the patient, we recommend that you test all of the patient’s samples in the same series to detect significant variations in titers of IgG anti-*Aspergillus* antibodies.

13- LIMITATIONS OF THE PROCEDURE

1. A negative result cannot exclude a diagnosis of aspergillosis.
   A diagnosis of aspergillosis can only be made after studying the clinical, therapeutic, radiological, cytological, direct mycological and serological results, necessarily interpreting each element taken in isolation with circumspection.
2. In an immunocompetent patient suspected of having aspergillosis, sample taken early on in the disease of the *Aspergillus* infection may show a negative result for detection of IgG anti-*Aspergillus*. A new assay carried out on a sample taken at a two or three week interval is therefore recommended.
3. The procedure and the interpretation of the results described for the Platelia™ *Aspergillus* IgG assay must be monitored when samples are tested for the presence of IgG anti-*Aspergillus* antibodies. We recommend that the kit user read the insert carefully before carrying out the assay. The protocol must be followed particularly closely in pipetting samples and reagents, washing the microplate and in timing incubation stages.
4. A false negative result may be obtained if the samples and the reagents are not added as indicated in the insert. In the event of procedural error, a new sample from the same patient must be tested.
5. Contamination of wells containing negative patient samples by wells containing positive patient samples or patient samples may occur if the contents of a well overflow into another well due to clumsy handling of the microplate or due to poor pipetting technique when adding reagents.
6. The performance results of Platelia™ *Aspergillus* IgG were not assessed using samples of serum or plasma from new-born infants or pediatric patients.
7. The performance of Platelia™ *Aspergillus* IgG were not established for manual reading and/or visual determination of the results.

14- EXPECTED VALUES

The prevalence of anti-*Aspergillus* IgG measured using the Platelia™ *Aspergillus* IgG test was evaluated using a panel of 129 samples from 64 French patients suffering from cystic fibrosis and presenting a risk of *Aspergillus* infection. Of the 129 samples, 53 proved positive and 12 intermediate, for a prevalence of 53/129 = 41.1% [95% CI: 32.5-50.1%] considering the intermediate results as negative and 65/129 = 50.4% [95% CI: 41.4-59.3%] considering the intermediate results as positive. In terms of patients, of the 64 tested, 29 had at least one positive sample and 5 had at least one intermediate sample and no positives, for a prevalence of 29/64 = 45.3% [95% CI: 32.8-58.3%] considering the intermediate results as negative and 34/64 = 53.1% [95% CI: 40.2-65.7%] considering the intermediate results as positive.

15- PERFORMANCE CHARACTERISTICS

A. Reproducibility studies

- Intra-assay precision (repeatability):

To evaluate intra-assay repeatability, a negative sample and five positive samples were tested 32 times for a given series. The titer, in AU/ml, was determined for each sample. The average of the titers, the standard deviation (SD) and the coefficient of variation (CV%) for each sample are given in the following table:

Intra-assay precision (repeatability)

N=32	Negative Sample	Weak positive sample No. 1	Weak positive sample No. 2	Weak positive sample No. 3	Medium positive sample	Strong positive sample
Average (AU/ml)	2.44	9.31	10.31	13.64	31.69	43.10
SD	0.067	0.320	0.218	0.387	0.939	1.546
CV %	**2.7%**	**3.4%**	**2.1%**	**2.8%**	**3.0%**	**3.6%**

- Inter-assay precision (reproducibility):

To evaluate inter-assay reproducibility, each of six samples (one negative and five positives) was tested in duplicate, in two series a day, over a total period of 20 days. The titer, in AU/ml, was determined for each positive sample. The negative sample is expressed in the form of a ratio.

The average of the concentrations or ratios, the standard deviation (SD) and the coefficient of variation (CV%) for each sample are given in the following table:

Inter-assay precision (reproducibility)

N=80	Negative Sample	Weak positive sample No. 1	Weak positive sample No. 2	Weak positive sample No. 3	Medium positive sample	Strong positive sample
Average (AU/ml)	1.88	3.60	6.99	12.34	32.49	51.65
SD	0.26	0.46	0.92	1.49	5.25	7.65
CV %	**13.8%**	**12.8%**	**13.1%**	**12.1%**	**16.2%**	**14.8%**

B. Cross reactions

Pathology	Number of samples tested	Number of positive samples
Anti-*Candida* antibodies	54	2*
Anti-ds-DNA antibodies	10	0
ANA positive	10	0
Myeloma IgG	10	0
Toxoplasma IgG	10	0
Human anti-mouse antibodies	12	0
HIV	10	0
Rheumatoid Factor	10	0

* The two sera that tested positive were confirmed with a commercial kit for detecting anti-*Aspergillus* IgG antibodies.

C. Linearity

The linear dynamic range of the Platelia™ *Aspergillus* IgG dosage was established between 2 and 80 UA/ml using dilution studies performed on 5 positive samples.

D. Clinical studies

The performance characteristics of the Platelia™ *Aspergillus* IgG kit were evaluated at 2 sites on a total of 499 samples from 329 patients.

SENSITIVITY

Sensitivity was determined using a panel of 277 samples from 2 sites located in France, broken down as follows:

- 129 sera from 64 patients suffering from cystic fibrosis and presenting high risks of allergic bronchopulmonary aspergillosis (ABPA) were tested at site 1.
- 148 sera from 43 patients with severe, chronic aspergillosis were tested at site 2.

Results for Site 1

The table below sums up the results obtained at site 1 for a population of patients suffering from cystic fibrosis and for whom the ABPA diagnosis was carried out on the basis of clinical data, with results obtained for total IgE, *Aspergillus* electrosyneresis, detection of *Aspergillus* antigens and detection of anti-*Aspergillus* IgG antibodies with a commercial EIA test other than Platelia™ *Aspergillus* IgG. The patients were classified in 4 categories: absence of ABPA, previous ABPA, suspected ABPA and confirmed ABPA [9, 11]. The absence of ABPA does not, however, exclude another *Aspergillus* pathology [12]. The patient's status with *Aspergillus* electrosyneresis or Platelia™ *Aspergillus* IgG was considered as positive when at least one of the patient's samples tested positive with the corresponding method. Otherwise, the status was considered intermediate if at least one of the patient's samples tested intermediate and negative if all the patient's samples tested negative.

Patient categories	Electrosyneresis results		Platelia™ *Aspergillus* IgG results				
	Status	Number of patients	Patient status			Positive (%) (intermediate patients considered as negative)	Positive (%) (intermediate patients considered as positive)
			Positive	Intermediate	Negative		
49 patients without ABPA	Negative	40	7 [1]	4 [2]	29	7/40 (17.5%) 95% CI [7.3-32.8%]	11/40 (27.5%) 95% CI [14.6-43.9%]
	Positive	9	8	1	0	8/9 (88.9%)*	9/9 (100.0%)*
5 patients with previous ABPA	Negative	5	5 [3]	0	0	5/5 (100.0%)*	5/5 (100.0%)*
	Positive	0	-	-	-	-	-
4 patients with suspected ABPA	Negative	2	2 [4]	0	0	2/2 (100.0%)*	2/2 (100.0%)*
	Positive	2	2	0	0	2/2 (100.0%)*	2/2 (100.0%)*
6 patients with confirmed ABPA	Negative	3	2 [5]	0	1	2/3 (66.7%)*	2/3 (66.7%)*
	Positive	3	3	0	0	3/3 (100.0%)*	3/3 (100.0%)*

[1]: 57% (4/7) of the positive results with Platelia™ Aspergillus IgG tested positive with another EIA kit marketed to detect anti-Aspergillus IgG.

[2]: 100% (4/4) of the intermediate results with Platelia™ *Aspergillus* IgG tested negative with another EIA kit marketed to detect anti-*Aspergillus* IgG.

[3]: 100% (5/5) of the positive results with Platelia™ *Aspergillus* IgG tested positive with another EIA kit marketed to detect anti-*Aspergillus* IgG.

[4]: 100% (2/2) of the positive results with Platelia™ *Aspergillus* IgG tested positive with another EIA kit marketed to detect anti-*Aspergillus* IgG.

[5]: 100% (2/2) of the positive results with Platelia™ *Aspergillus* IgG tested positive with another EIA kit marketed to detect anti-*Aspergillus* IgG.

* : The 95% confidence interval could not be calculated due to insufficient sample size.

Results for Site 2

The table below sums up the results obtained with a sample population of patients suffering from severe chronic aspergillosis recruited on the basis of compatible pulmonary imaging, expectoration cultures positive for *Aspergillus*, and *Aspergillus*-positive serological tests using immuno-electrophoresis (IEP).

• Results by sample

Patient categories	IEP results		Platelia™ *Aspergillus* IgG results				
	Status	Number of samples	Positive	Intermediate	Negative	Sensitivity (intermediate patients considered as negative)	Sensitivity (intermediate patients considered as positive)
Severe chronic aspergillosis	Positive	109	105	3	1	96.3% 95% CI [90.8-99.0]	99.1 % 95% CI [95.0-100]
	Intermediate	22	15	4	3	68.2 % 95% CI [45.1-86.1]	86.4 % 95% CI [65.1-97.1]
	Negative	17	6	5	6	35.3 % 95% CI [14.2-61.7]	64.7 % 95% CI [38.3-85.8]

• Results by patient

The patient's status with *Aspergillus* immunoelectrophoresis or Platelia™ *Aspergillus* IgG was considered positive when at least one of the patient samples tested positive with the corresponding method. Otherwise, the status was considered intermediate if at least one of the patient samples tested intermediate and negative if all the patient samples tested negative.

Patient categories	IEP results		Platelia™ *Aspergillus* IgG results				
	Status	Number of patients	Positive	Intermediate	Negative	Sensitivity (intermediate patients considered as negative)	Sensitivity (intermediate patients considered as positive)
Severe chronic aspergillosis	Positive	40	38	1	1	95.0% 95% CI [83.1-99.4]	97.5 % 95% CI [86.8-99.9]
	Negative	3	1	1	1	33.3 % *	66.7 % *

*: The 95% confidence interval could not be calculated due to insufficient sample size.

SPECIFICITY

Specificity was determined using a panel of 222 samples from 222 patients hospitalized at site 1 (200 samples) and site 2 (22 samples) and who had no symptoms of *Aspergillus* infection.

Population tested / site	Number of samples	Negative	Intermediate	Positive	Specificity (intermediate patients considered as positive)	Specificity (intermediate patients considered as negative)
Site 1	200	199	1	0	99.5% 95% CI [97.2%-100.0%]	100% 95% CI [98.2-100.0%]
Site 2	22	22	0	0	100% 95% CI [84.6%-100.0%]	100% 95% CI [84.6%-100.0%]
Total	222	221	1	0	99.6% 95% CI [97.5-100.0%]	100% 95% CI [98.3-100.0%]

16. QUALITY CONTROL OF THE MANUFACTURER

All manufactured reagents are prepared according to our Quality System, starting from reception of raw material to commercialization of the final product. Each lot is submitted to quality control assessments and is released to the market only after conforming to pre-defined acceptance criteria.

The records related to production and controls of each single lot are kept within Bio-Rad.

17. BIBLIOGRAPHY

1. **Agarwal, R.** 2009. Allergic bronchopulmonary aspergillosis. Chest **135** (3): p 805-826.
2. **Agarwal, R., Nath, A., Aggarwal, A. N., Gupta, D., Chakrabarti, A.** 2009. *Aspergillus* hypersensitivity and allergic bronchopulmonary aspergillosis in patients with acute severe asthma in a respiratory intensive care unit in North India. Mycoses **24**.
3. **Centeno-Lima, S., de Lacerda, J. M., do Carmo, J. A., Abecasis, M., Casimiro, C., Exposto, F.** 2002. Follow-up of anti-*Aspergillus* IgG and IgA antibodies in bone marrow transplated patients with invasive aspergillosis. Journal of clinical laboratory analysis **16**: p156-162.
4. **Denning, D. W.** 2001. Chronic forms of pulmonary aspergillosis. Clinical microbiology and infection **7** (Suppl 2): p25-31.
5. **Latzin, P., Hartl, D., Regamey, N., Frey, U., Schoeni, M. H., Casaulta, C.** 2008. Comparison of serum markers for allergic bronchopulmonary aspergillosis in cystic fibrosis. Eur. Respiratory Journal **31**: p36-42.
6. **Pagella, F., Matti, E., De Bernardi, F., Semino, L., Cavanna, C., Marone, P., Farina, C., Castelnuovo, P.** 2007. Paranasal sinus fungus ball: diagnosis and management. Mycoses **50**: p451-456.

7. **Sarfati, J., Monod, M., Recco, P., Sulahian, A., Pinel, C., Candolfi, E., Fontaine, T., Debeaupuis, J.P., Tabouret, M., Latgé, J.P.** 2006. Recombinant antigens as diagnostic markers for aspergillosis. Diagnostic microbiology and infectious disease **55**: p. 279-291.
8. **Schubert, M. S.** 2009. Allergic fungal sinusitis: pathophysiology, diagnosis and management. Medical Mycology p1-7.
9. **Shah, A.** 2008. *Aspergillus*-associated hypersensitivity respiratory disorders. Indian journal of Chest disease and allied sciences **50**: p117-128
10. **Shah, R., Vaideeswar, P., Pandit, S. P.** 2008. Pathology of pulmonary aspergillomas. Indian journal of pathology and microbiology **51** (3): p342-345.
11. **Thia, L. P., Balfour Lynn, I. M.** 2009. Diagnosing allergic bronchopulmonary aspergillosis in children with cystic fibrosis, Paediatric Respiratory Reviews **10**: p37–42
12. **Tillie-Leblond, I., Tonnel, A. B.** 2005. Allergic bronchopulmonary aspergillosis. Allergy **60**: p1004-1013.
13. **Virnig, C., Bush, R. K.** 2007. Allergic bronchopulmonary aspergillosis: a US perspective. Current opinion in Pulmonary Medicine **13**: p67-71.

(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 ταμάτια/ πρόσωπο. ΣΕ ΠΕΡΙΠΤΩΣΗ ΕΠΑΦΗΣ ΜΕ ΤΑ ΜΑΤΙΑ: Ξεπλύνετε προσεκτικά με νερό για αρκετά λεπτά. Εάν υπάρχουν φακοί επαφής, αφαιρέστε τους, εφόσον είναι εύκολο. Συνεχίστε να ξεπλένετε. ΣΕ ΠΕΡΙΠΤΩΣΗ ΚΑΤΑΠΟΣΗΣ: Ξεπλύνετε το στόμα. ΜΗΝ προκαλέσετε εμετό. ΣΕ ΠΕΡΙΠΤΩΣΗ ΕΠΑΦΗΣ ΜΕ ΤΟ ΔΕΡΜΑ (ή με τα μαλλιά): Αφαιρέστε αμέσως όλα τα μολυσμένα ενδύματα. Ξεπλύνετε το δέρμα με νερό/στο ντους. Εάν παρατηρηθεί ερεθισμός του δέρματος ή εμφανιστεί εξάνθημα: Συμβουλευθείτε/ Επισκεφθείτεγιατρό. Απορρίψτε τα περιεχόμενα/ δοχείο σύμφωνα με τους τοπικούς/εθνικούς/διεθνείς κανονισμούς.

(HR)

Opasnost

Uzrokuje teške opekline kože i ozljede oka. Može izazvati alergijsku reakciju na koži.

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

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

(PL)

Niebezpieczeństwo

Powoduje poważne oparzenia skóry oraz uszkodzenia oczu . Może powodować reakcję alergiczną skóry.
Stosować rękawice ochronne/odzież ochronną/ochronę oczu/ochronę twarzy. W PRZYPADKU DOSTANIA SIĘ DO OCZU: Ostrożnie płukać wodą przez kilka minut. Wyjąć soczewki kontaktowe, jeżeli są i można je łatwo usunąć. Nadal płukać. W PRZYPADKU POŁKNIĘCIA: wypłukać usta. NIE wywoływać wymiotów. W PRZYPADKU 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

Provoacă 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.

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

CE

2013/11
code: 881123