Aspergillus galactomannan

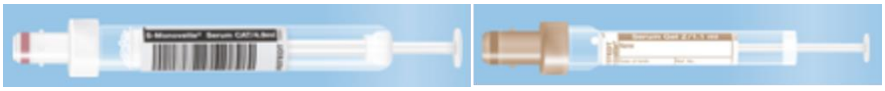
Platelia assay for *Aspergillus* galactomannan circulating antigen in serum and other body fluids: this test is indicated for presumptive diagnosis of *Aspergillus* infection.

General information

Turnaround time: This assay is performed every day, Monday-Friday. Turnaround time: 95% within one weekday.

Sample type/container:

Blood:



- 4.9 ml clotted blood
- Serum tube (Sarstedt S-Monovette white cap) or serum gel tube (brown cap). Blood collected in EDTA tubes will be rejected.
- Please do not remove the cap before sending for testing nor share the sample to avoid laboratory contamination.

Bronchoalveolar lavage fluid (BALF):

- Send minimum of 2 ml collected into appropriate UKCA/CE-marked sterile leakproof containers.
- **Do not** send containers with trap tubing still attached. These samples are prone to leaking and contamination. The trap tubing **must** be replaced with a secure screw cap lid prior to placing in the specimen bag.

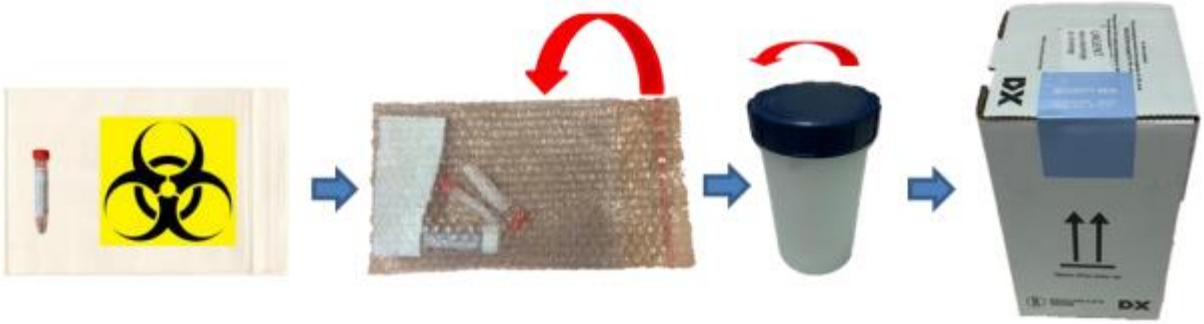
Other sample types:

- The test is only validated for blood/serum and BALF
- The test can be performed on other body fluids such as cerebrospinal fluid (CSF) but clear evidence-based guidance for interpretation of the results cannot be provided.

Transportation

- Samples should be placed into a plastic Ziploc bag, sealed, and then placed into another sealed plastic Ziploc bag (preferably with a biohazard label on the outside), as shown below.

- Category B transport boxes or an appropriate transport bag (i.e., one which adheres to regulations governing the transportation of diagnostic specimens) must be used for transport by road or between Manchester University Foundation Trust sites (but are not necessary within Wythenshawe hospital grounds).
- Please see below for packaging requirements.



For more information - https://mrcm.org.uk/sample-collection/

Laboratory Information

Biological interval/clinical decision values:

The Platelia galactomannan (GM) test results are expressed as an index value and are reported for blood as negative or positive, and for BAL negative, weak positive, or positive – with the index value provided.

Interpretation of values depends on the sample type:

Blood/serum: GM index values of > 0.5 are interpreted as positive.

The accuracy of the result may be affected if the blood sample is more than 5 days old or if the serum sample is more than 2 days old.

BALF: GM index values >1.0 are interpreted as positive. Index values 0.5-1.0 have a lower predictive value than values >1.0 and are interpreted as weakly positive. Further sampling is recommended.

The accuracy of the result may be affected if the BALF sample is more than 1 day old.

A single negative result does not rule out the diagnosis of invasive aspergillosis (IA). Repeat testing and additional alternative modalities of testing are recommended if the result is negative, but the disease is suspected.

Conversely, a single positive GM value does not solely constitute the diagnosis of IA and additional diagnostic tests and/or testing of additional samples is needed. Recent data suggests that the combination of two weak/positive GM test results, one in serum/plasma (≥ 0.7) and one in BALF (≥ 0.8), may suggest the presence of IA.

Cerebrospinal fluid (CSF): The test is **not** validated for CSF samples. The cut-off value for this sample type has not been established but values >0.5 and ≥1 have been used. Measuring the serum GM/CSF GM ratio may be useful as high galactomannan levels in CSF are indicative of intrathecal infection.

Sputum: The test is **not** validated for sputum samples. The cut-off value for this sample type has not been established. High values (>1) should only trigger further investigations in the presence of clinical suspicion.

Clinical Information

No specific time of optimal collection. First clinical indication or monitoring of invasive aspergillosis.

In general, the performance of the GM test varies between patient groups and sample types. Blood galactomannan has high specificity in neutropenic haematology-oncology patients and solid organ transplant patients, whilst it has very low sensitivity in non-neutropenic patients. High sensitivity and specificity can be achieved by testing samples collected from the likely site on infection (mainly lungs, BALF). BALF is the preferred sample type in non-neutropenic patients.

This test should be used in conjunction with other diagnostic procedures such as high-volume fungal culture, *Aspergillus* PCR, histological examination of biopsy specimens and radiographic evidence, as an aid in the diagnosis of invasive aspergillosis, in specific clinical contexts (e.g., neutropenic patients or patients treated with immunosuppressants).

This test can also be used as an aid to monitor antifungal treatment efficacy based on galactomannan index evolution.

In appropriate clinical settings, screening may be considered to monitor for evidence of elevated levels of galactomannan, which provides a potential surrogate marker for invasive *Aspergillus* disease (depending on sample type tested).

For clinical advice and guidance, please contact the laboratory via Hive or by email (mrcm@mft.nhs.uk).

Limitations:

Possible causes of false negatives:
The Platelia *Aspergillus* galactomannan assay may exhibit reduced detection of galactomannan in patients with chronic granulomatous disease and hyper IgE (Job's) syndrome.

The concomitant use of mould-active anti-fungal prophylaxis or therapy may result in reduced sensitivity with the galactomannan test.

Blood galactomannan has very low sensitivity in non-neutropenic patients. BAL is the preferred sample type in these patients when pulmonary aspergillosis is suspected.

Possible causes of false positives:
Serum specimens stored inappropriately or tested with a delay may give false positive results due to contamination with fungi and/or bacteria.

The performance of the Platelia *Aspergillus* galactomannan assay has not been evaluated in neonatal samples. There is a higher incidence in the number of false positive galactomannan results reported in European literature in samples from the neonatal population.

Other genera of fungi such as *Penicillium*, *Fusarium*, *Alternaria, Paecilomyces*, *Geotrichum* and *Histoplasma* have shown reactivity with the monoclonal antibody used in the assay for the detection of *Aspergillus* GM. Histoplasmosis should be considered in patients with travel history to endemic areas.

Positive reactions in the absence of clinical signs may be observed in patients receiving products containing galactomannan, either parenterally or orally (if there is an alteration of the intestinal barrier), due to production processes that include fungal microorganism-based fermentation.

For example, galactofuranose, which can be present in various foods, particularly cereals, cereal products, cow milk formula and cream desserts, may produce a positive result in patients with a damaged or immature intestinal barrier. Dietary factors must therefore be considered as a potential source of antigenemia in these patients particularly in the absence of clinical signs and symptoms of invasive aspergillosis.

Historically, positive test results were reported in patients receiving ß-lactams such as piperacillin/tazobactam, amoxicillin with clavulanic acid, and ampicillin but this has been addressed now in the manufacturing processes of these and other antibiotics. Therefore, these antibiotics are currently not a significant source for false-positive test results.

The Platelia *Aspergillus* galactomannan test may exhibit false positive results with serum specimens when digestive enzymes of fungal origin, like Nortase, are used for enzyme substitution therapy in exocrine pancreatic insufficiency in ICU patients.

References:

BioRad Platelia Aspergillus Ag, SEMI-QUANTITATIVE IMMUNOENZYMATIC SANDWICH MICROPLATE ASSAY FOR THE DETECTION OF ASPERGILLUS GALACTOMANNAN ANTIGEN IN ADULT AND PEDIATRIC SERUM SPECIMENS AND BRONCHOALVEOLAR LAVAGE (BAL) FLUID SPECIMENS, version 0001315 - 2023/07.

Toine Mercier et al., Defining Galactomannan Positivity in the Updated EORTC/MSGERC Consensus Definitions of Invasive Fungal Diseases, *Clinical Infectious Diseases*, Volume 72, Issue Supplement_2, 15 March 2021, Pages S89–S94, https://doi.org/10.1093/cid/ciaa1786.

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