



**3rd
European
Conference on
Infections in
Leukemia**

**Non-culture-based diagnostic procedures
for *Aspergillus* infections**

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Galactomannan: assay characteristics

Description of the test:

- The target of the Platelia *Aspergillus* is the galactofuranose side chains of the galactomannan molecule.
- Galactomannan is released by all *Aspergillus* species.
- Galactomannan detection by Platelia *Aspergillus* is not specific for *Aspergillus* spp. but may be produced by other fungi (a list is provided).
- Galactomannan detection in plasma is equivalent to that in serum
- Samples for galactomannan detection may be stored at room temperature, 4°C, -20°C or -80°C.
- The heating step is critical to the success of the assay.



Galactomannan: recommendations for use in adults

- The manufacturer recommends a cut-off of 0.5 for the Platelia *Aspergillus* in serum
- Detection of galactomannan in BAL fluid can be used to support the diagnosis of invasive aspergillosis in neutropenic and non-neutropenic patients. Pending a recommended cut off by the manufacturer, a cut-off of 1.0 is recommended (BIII)
- Detection of galactomannan in CSF can support the diagnosis of central nervous system aspergillosis. Pending a recommended cut-off by the manufacturer, a cut-off of 0.5 is recommended (BIII)
- Experience with galactomannan detection in pleural fluid, sputum or urine is insufficient to make recommendations (CIII)



Galactomannan: recommendations for a strategy in adults

- **Prospective monitoring of serum is a feasible approach for adult neutropenic patients undergoing intensive chemotherapy for leukemia or receiving an allogeneic stem cell transplantation for the early diagnosis of invasive aspergillosis (All) [Note: Plasma may also be used (CIII)]**
- **Galactomannan monitoring is recommended every three to four days for patients admitted to hospital (All)**
- **Persistent galactomannan antigenaemia during therapy is a poor prognostic sign and should prompt a reassessment of the management of the patient (BII)**
- **A diagnostic driven strategy that incorporates galactomannan monitoring should be combined with high resolution CT imaging, appropriate clinical and microbiological evaluation to diagnose invasive aspergillosis early. A single sample with a galactomannan index of ≥ 0.7 or 2 consecutive samples with an index of ≥ 0.5 should prompt a thorough diagnostic work-up (All)**



Galactomannan: false-positivity

- Concomitant administration of some batches of the beta-lactam antibiotics piperacillin/tazobactam, amoxicillin-clavulanate and ampicillin
- Cross-reactivity with fungal species other than *Aspergillus sp* responsible for invasive fungal disease including *Penicillium marneffeii*, *Histoplasma capsulatum*, *Cryptococcus neoformans*, *Trichosporon sp.*
- Cross-reactivity with transfused blood or antiglobulin sera
- Cyclophosphamide
- Mucositis
- Paediatrics - milk-based diet, nutrient supplement containing soybean proteins
- Neonates - *Bifidobacterium bifidum*



Galactomannan: factors affecting assay performance

Epidemiological factors (*Pfeiffer et al, 2006 Clin Inf Dis, 42: 1417-27*)

- Patient population**
- Sampling strategy**
- Definition of a positive result**
- Definition of invasive aspergillosis**
- Prevalence of invasive aspergillosis**
- Cut-off threshold**
- Laboratory experiences**

Biological factors (*Mennink-Kersten et al, 2004 Lancet Infect Dis, 4: 349-57*)

- Site of infection**
- Aspergillus* species causing infection**
- Microenvironment at the site of infection (nutrients, oxygen supply, pH)**
- Exposure to antifungal agents**
- Molecular configuration of the galactomannan released**
- Underlying disease and degree of immune suppression**
- Renal clearance, hepatic metabolism**
- Presence of galactomannan antibodies**
- Storage of the sample**
- Sample pretreatment procedure**



PCR recommendations

The current status of the technical and clinical validation of PCR for *Aspergillus* in blood and other fluids does not currently allow for a recommendation for clinical use.

The technical recommendations of the European Aspergillus PCR Initiative (EAPCRI) for processing aspergillus PCR have been published after the ECIL 3 meeting and are those recommended by ECIL

Aspergillus PCR: one step closer towards standardisation

L White, S Bretagne, L Klingspor, WJG Melchers, E McCulloch, B Schulz, N Finnstrom, C Mengoli, RM Barns, JP Donnelly, J Loeffler
J Clin Microbiol, Epub ahead of print Feb. 10, 2010

