# ECMM Excellence Centers
# Quality Audit

| | |
|---|---|
| **Person in Charge** | |
| **Department** | |
| **Head of Department** | |
| **1st ECMM Inspector** | |
| **2nd ECMM Inspector** | |
| **Inspection Date** | |

| **Application for*** | | **Decision/Recommendation*** | |
|---|---|---|---|
| Blue Status (ECMM Fungal Center) | ☐ | Blue Status (ECMM Fungal Center) | ☐ |
| Silver Status (ECMM Excellence Center) | ☐ | Silver Status (ECMM Excellence Center) | ☐ |
| Gold Status (ECMM Excellence Center) | ☐ | Gold Status (ECMM Excellence Center) | ☐ |
| Diamond Status (ECMM Excellence Center) | ☐ | Diamond Status (ECMM Excellence Center) | ☐ |

*Requirements are given in Appendix 1

1st ECMM Inspector  2nd ECMM Inspector  Applicant

**Purpose**

The intent of the ECMM Excellence Cetner Programme is to increase visibility of excellent centers and to improve patient care.

**Requirements**

The audit takes place by collecting data on how laboratory diagnosis is made and on how clinical management of invasive fungal infections is effectively executed.

As a basis of the laboratory audit, the best practice recommendations for the diagnosis of serious fungal diseases will be used (Cuenca-Estrella M et al. CMI 2012;18:9-18; Schelenz S et al. Lancet Infect Dis. 2015;15:461-474; Ullmann AJ et al. CMI 2018; 24:e1-e38; Cornely OA et al. Lancet Infect Dis. 2019; 19:e405-421; Chen SCA et al. Lancet Infect Dis. 2021;21:e375-e386; Hoenigl M et al. Lancet Infect Dis. 2021;21:e246-e257).

The minimum requirements for the **Blue Status** (ECMM Fungal Centers, possibly ECMM Excellence Center candidates) for laboratories consist of:

- Identification of medical important yeasts and moulds
- Susceptibility testing on yeasts and moulds according to standard procedures
- Performance of antigen ELISA for *Aspergillus* or equivalent assay
- Cryptococcal antigen test

The clinical minimum requirements for the **Blue Status** in part depend on the type of patients cared for.

- Timely CT scan in immunosuppressed patients with suspected pneumonia
- Timely CT or MRI scan in immunocompromised patients with suspected brain infection
- Timely bronchoscopy and BAL
- Access to azoles, amphotericin B, and an echinocandin
- Access to appropriate surgery
- Access to second level ICU

**Silver Status**: Excellence in either laboratory mycology **or** clinical mycology. 2/3 of the practice recommendations according to the audit plan should be implemented.

**Gold Status:** Excellence in both, laboratory mycology **and** clinical mycology.

**Diamond Status:** Gold Status **and** participation in ECMM endorsed clinical or epidemiological studies.

**Applicants should send the audit plan to the auditors two weeks before the audit takes place.**

| | *Yes* | *No* | *Comments* |
|---|---|---|---|
| ***Panel 1: Microbiology best practice recommendations which should be available*** | | | |
| **Microscopy and stains** | | | |
| • Fluids from usually sterile sites and bronchoalveolar lavage (BAL) from patients with suspected infection should be examined by direct microscopy with suitable methods for fungal detection. | | | |
| • Optical brighteners are used for microscopy on all samples from patients with suspicion of invasive fungal infection. | | | |
| • Direct fluorescent –(antibody) staining, PCR, or both is available for patients with suspected pneumocystis infection in induced sputum or BALs. | | | |
| • India ink staining of cerebrospinal fluid and/or Cryptococcus capsule antigen (CRAG) testing is available. | | | |
| **Culture and identification** | | | |
| • Bronchoscopy fluids and other specimens are cultured in suitable media at different temperatures to support fungal growth. | | | |
| • All significant clinical isolates of Aspergillus & other fungi from patients who receive antifungal treatment are identified to species complex level. | | | |
| • All fungi (yeasts and moulds) obtained from sterile sites, including blood and continuous ambulatory peritoneal dialysis fluids, and intravenous line tips are identified to species complex level. In addition, susceptibility tested with a scientifically accepted method **or** reference method is done (EUCAST/CLSI). In severe immunosuppressed patients, bronchoscopy fluid and paranasal sinus material should be regarded as sterile in this context for all fungi except Candida spp. | | | |
| • If direct microscopy is positive for fungal mycelia all cultured fungi are potentially clinically relevant. All Aspergillus isolates from patients with allergic bronchopulmonary aspergillosis, aspergilloma, chronic aspergillosis or acute invasive aspergillosis should be susceptibility tested for antifungals used for treatment if therapy is initiated; isolates should be stored for at least 6 months in case additional susceptibility testing is needed later. | | | |
| • In immunosuppressed patients, fungi cultured from vascular-device tips are identified to species level and reported. | | | |
| **Respiratory specimens** | | | |
| • BAL fluid is recommended for diagnosis of pulmonary invasive fungal disease in immunosuppressed patients or with suspicion of suffering from invasive aspergillosis or invasive fungal infection. | | | |

| | *Yes* | *No* | *Comments* |
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| • Respiratory and fluid samples should be concentrated by centrifugation at 1000 g or greater for at least 10 min or with the cytocentrifuge before microscopy.<br>• Respiratory samples should be liquified, especially for detection of *Pneumocystis jirovecii.* | | | |
| • Isolation of *Aspergillus* spp from respiratory samples: the laboratory provides interpretative comments according to patient risk group and likelihood of invasive, chronic, or allergic disease. | | | |
| • Sputum samples could be obtained for detection of respiratory fungi, especially in chronic cases of aspergillosis. | | | |
| **Cerebrospinal fluid (CSF) specimens** | | | |
| • All CSF specimens that are from patients with suspicion of cryptococcal meningitis (e.g. immunocompromised patients, patients with sarcoidosis or cancer, or who show abnormal concentrations of glucose, protein, or leucocytes without an adequate explanation) must be cultured and antigen tested for *Cryptococcus neoformans*; all bacterial plates should be incubated for a minimum of 5 days and fungal media incubated at 30°C for up to 28 days. | | | |
| **Fungal serological and molecular testing** | | | |
| • Serum samples from immunocompromised patients with presentations consistent with cryptococcal meningitis for whom a CSF specimen is not available (e.g., cases in which lumbar puncture is contraindicated) should be tested for Cryptococcus spp antigen (CRAG).<br>Time from sampling to result reported should be within 2 working days. | | | |
| • Galactomannan screening of serum (2-3 times per week) from patients with haematological malignancies at high risk of invasive aspergillosis in those not receiving mould-active prophylaxis.<br>Time from sampling to result reported should be within 2 working days. | | | |
| • Galactomannan testing of BAL from patients at high risk of invasive aspergillosis should be considered.<br>Time from sampling to result reported should be within 2 working days. | | | |
| • β-D-glucan screening of serum from patients at high risk of invasive fungal disease could be considered; a negative result has a high negative predictive value, enabling invasive fungal disease to be excluded.<br>Time from sampling to result reported should be within 2 working days. | | | |
| • PCR screening of serum for *Aspergillus* from patients at high risk of invasive fungal disease could be considered; a negative result | | | |

| | *Yes* | *No* | *Comments* |
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| has a high negative predictive value, enabling invasive fungal disease to be excluded. | | | |
| • Combination testing with *Aspergillus* PCR plus another antigen test improves the positive and negative predictive values and diagnosis of invasive fungal disease, hence should be considered. | | | |
| • PCR testing of biopsy samples should be considered in case fungal hyphae are detected. | | | |
| • Patients with pulmonary cavities of uncertain cause (with or without an aspergilloma) should have serum samples tested for *Aspergillus*-specific IgG. | | | |
| • Patients with suspected allergic bronchopulmonary aspergillosis should have serum samples tested for total IgE and *Aspergillus*-specific IgE. | | | |
| **Antifungal drug-susceptibility testing** | | | |
| • Isolates of *Candida* spp and yeasts from sterile sites, or from patients not responding to therapy at a minimum should have their susceptibility tested against a standard panel of antifungals or the specific drug given. | | | |
| • Significant clinical isolates of *Aspergillus* species should have their susceptibility tested against antifungals used. | | | |
| • Reporting MIC data should include whether the values given display epidemiological (ECOFFs) or clinical breakpoints; there is need to underline that ECOFFs divide the wild type (WT) and non-wild type (NWT) population; NWT harbour one or more resistance mechanisms but, depending on the values of the clinical breakpoints, WT and NWT fungi may or may not respond clinically to treatment with the agent. | | | |
| **Therapeutic drug monitoring** | | | |
| • Therapeutic drug monitoring of itraconazole, voriconazole, and posaconazole (oral solution only) is recommended by guidelines. Specifically, voriconazole monitoring is needed in most patients, and certainly in children, including repeat monitoring after dose changes and shift from intravenous to oral treatment; dose optimization during long-term therapy needs such monitoring. Time from sampling to result reported should be within 2 working days. | | | |
| • Blood concentration monitoring is recommended for all patients receiving flucytosine. Time from sampling to result reported should be within 2 working days. | | | |
| **Clinical requests and reporting** | | | |
| • Background information regarding the patient immune status should be available for any interpretation of the results obtained. | | | |

| | *Yes* | *No* | *Comments* |
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| • All intravascular devices should be removed promptly if clinically feasible after diagnosis of candidaemia irrespective of the species identified. | | | |
| • All new fungaemia, positive results of microscopy on sterile tissues or fluids, and positive cryptococcal antigen and galactomannan results should be communicated by laboratory staff to clinicians within 2 h of their availability. | | | |
| ***Panel 2: Histopathology best practice recommendations which should be available**** | | | |
| **Specialized stains** | | | |
| Specialized stains should be done in parallel with standard stains if mycosis or another infection is to be assessed or excluded. | | | |
| • Standard stain: haematoxylin and eosin (H&E) on histopathology slides; Giemsa or Papanicolaou on smears. | | | |
| • Triple set of stains: Ziehl–Neelsen stain for acid-fast organisms; Gram stain for bacteria, fungi, and others; Grocott silver stain, or periodic acid–Schiff, Fontana-Masson to highlight fungi. | | | |
| **Reporting of results** | | | |
| Report fungal morphology (yeasts hyphae, mixed), including the following: | | | |
| • Whether a yeast is small, medium, or large. | | | |
| • Whether a yeast has cross walls or septa (i.e., is splitting rather than budding). | | | |
| • Whether a hyphal form has usual width, or has a dilated, bizarre shape, how the fungus branches (*Aspergillus* like or not). | | | |
| • Whether H&E-stained fungi are pigmented and brown or are unpigmented and colourless or pale blue. | | | |
| Positive results should be telephoned to clinicians immediately. Review of the stains by a mycologist is encouraged in case of a positive histology. | | | |
| ***Panel 3: Radiology best practice recommendations which should be available*** | | | |
| **Patients with leukaemia, and patients who have undergone haemopoietic stem cell or solid organ transplantation:** All patients with acute leukaemia or other hematological malignancy and patients who have undergone haemopoietic stem cell transplantation, who are, or who have been, profoundly neutropenic (<500 neutrophils/µL) with any of the following signs or symptoms should have a high-resolution (or spiral) or, preferably, multidetector CT scan of the entire thorax within 24-48 h, with immediate consultant review: | | | |
| • New cough, chest pain, or haemoptysis | | | |
| • Abnormal chest radiograph | | | |
| • New positive culture of an *Aspergillus* spp or other mould from any site | | | |

| | *Yes* | *No* | *Comments* |
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| • Microscopic evidence of hyphae in any respiratory sample | | | |
| • Unresolved temperature under antibiotics | | | |
| • Positive fungal biomarkers (i.e., galactomannan, β-D glucan, or PCR): All solid organ transplant recipients who test positive by microscopy, PCR, galactomannan, or culture of Aspergillus spp or other mould should have a CT scan of the chest (as above) within 24-48 h. | | | |
| **Immunocompromised patients with new neurological features**<br>All immunocompromised patients with new neurological features (e.g., change in mental status, seizure, stroke, or persistent headache) or possible or proven meningitis should have MRI of the brain within 48 h (or if not possible, a contrast-enhanced CT scan). | | | |
| **Suspected invasive fungal sinus infection**<br>All patients with suspected invasive fungal paranasal sinus infection receive a non-contrast CT scan within 24-48 h. | | | |
| **Suspected disseminated fungal infection**<br>Patients undergoing investigation for disseminated fungal infection should have an MR or dual-phase CT scan of the abdomen within 24-48 h. | | | |
| A low threshold for repeat scanning in patients with suspected cerebral and hepatosplenic fungal infection is in place. | | | |
| **Suspected pneumocystis infection in patients without HIV**<br>In patients not infected with HIV and possible *Pneumocystis* pneumonia, a CT scan of the chest should be made for differential diagnoses within 24-48 h, in combination with respiratory sample testing for *Pneumocystis jirovecii.* | | | |
| **Participation in external quality control programmes for identification and antifungal susceptibility testing of fungi with good performance.** | | | |
| ***Panel 4: Clinical best practice recommendations which should be available*** | | | |
| **Treatment infrastructure** | | | |
| • Access to all antifungal drug classes incl. triazoles, echinocandins, liposomal or lipid complex amphotericin B. | | | |
| • Access to experienced thoracic, visceral and neurosurgery for diagnosis and treatment of IFD. | | | |
| • Access to a second level ICU. | | | |
| **Diagnostic infrastructure**<br><br>**Access to timely diagnostic intervention.** | | | |
| • CT scanning within 24 hours. | | | |
| • CT guided biopsy within 24-72 hours. | | | |

| | *Yes* | *No* | *Comments* |
|---|---|---|---|
| • MRI scanning within 24 hours. | | | |
| • Bronchoscopy within 24-48 hours. | | | |
| **Research infrastructure** | | | |
| • Patient enrolment in clinical trials. | | | |
| • Participation in registry studies. | | | |
| **Experienced in and currently actively consulting in IFD** | | | |
| • National patient referrals and to consult physicians from external centers. | | | |
| • Consultation from other ECMM EC. | | | |
| ***Panel 5: Publishing, teaching, education, and others*** | | | |
| • Active publishing in the field of IFD. | | | |
| • Active teaching and lecturing locally and nationally. | | | |
| • Networking and multidisciplinary sessions within the hospital. | | | |
| • Presence of a multidisciplinary group within the hospital being involved in managing fungal infections (i.e., ID, Clinical Mycologist, Clinical pharmacologist, …) and /or antifungal stewardship. | | | |
| ***Panel 6: Clinical and epidemiological studies*** | | | |
| • Collaboration and networking with other appointed ECMM EC. | | | |
| • Active support of studies endorsed by ECMM. | | | |
| • Studies the applicant currently contribute to. | | | |

**Additional Comments:**