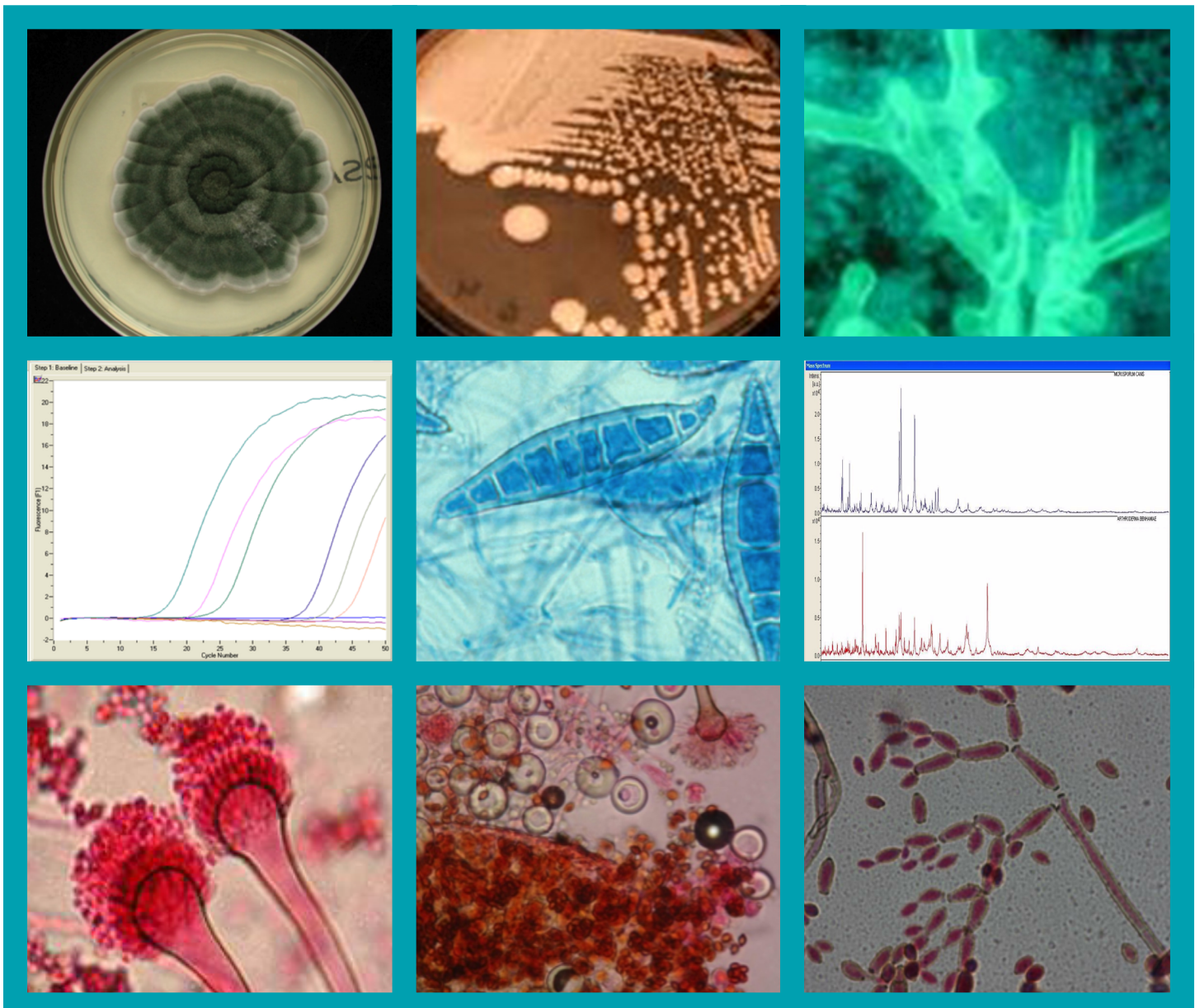




Public Health
England

Mycology Reference Laboratory

Service User Handbook



The PHE Mycology Reference Laboratory (MRL) is situated at the PHE South West Laboratory in Bristol. It is part of the Microbiology Services Division.

The MRL provides a comprehensive service for the diagnosis and management of fungal infections through the provision of specialist laboratory services and expert clinical and technical advice.

The MRL also houses the National Collection of Pathogenic Fungi (NCPF), which is the only culture collection in the UK specialising in fungi pathogenic to humans and animals.

AVAILABLE SERVICES:

Clinical Services

- We provide advice by telephone to ensure selection of the most appropriate test or specimen types for particular patients and assist with the interpretation of results
- We can also provide guidance on the clinical management of individual cases

Reference Services

- **Identification**

Moulds (including dermatophytes)
Unusual yeasts
Dimorphic fungal pathogens

- **Reference antifungal drug susceptibility testing of yeasts and moulds**

These tests are carried out as confirmatory tests for isolates producing equivocal or unexpected results.

- **Serological tests**

Serology of non-indigenous mycoses:
Histoplasmosis
Coccidioidomycosis
Blastomycosis
Paracoccidioidomycosis

- **Histological examination of referred slides**

Referred Tests (*charged*)

- **Identification of yeast and mould isolates**
- **Antifungal susceptibility testing of yeasts:**

anidulafungin, amphotericin, caspofungin, clotrimazole, econazole, fluconazole, flucytosine, itraconazole, ketoconazole, micafungin, miconazole, nystatin, posaconazole, voriconazole

- **Antifungal drug susceptibility testing of moulds:**

amphotericin, caspofungin, clotrimazole, griseofulvin, itraconazole, natamycin, posaconazole, terbinafine, voriconazole. Other drugs may be available on request, please contact the MRL.

- **Antifungal drug assays:**

amphotericin, fluconazole, flucytosine, itraconazole, posaconazole, voriconazole
Please contact the MRL prior to sending samples for amphotericin or fluconazole assays.

- **Serological tests:**

- Tests for antibodies to *Aspergillus*, *Candida*, *Thermophilic actinomycetes* (farmer's lung) and avian allergens.
- Tests for *Aspergillus* (galactomannan), *Candida* (mannan) and *Cryptococcus* antigens.
- Beta 1-3 Glucan antigen detection for invasive fungal infections. (NB: this test has a very high negative predictive value)

- **Diagnostic PCR on blood, fluids and tissue**

- **Microscopy and culture of clinical specimens**

- **Environmental Sampling (please telephone for details)**

- **Typing of common fungal pathogens**

Laboratory Turn-around Times (from receipt of sample)

All reports are sent by first class mail. Urgent results can be telephoned to laboratories on request provided we have an appropriate contact name and current telephone number. Results are available via an electronic link (please telephone for information).

Test Type	TAT (days)	
	Min	Mean
Aspergillus antibodies	2	3.1
Aspergillus antigen (galactomannan)	1	1.2
Avian antibodies	5	6.9
Beta 1-3 Glucan	1	3
Candida antibodies	2	3.5
Candida antigen (mannan)	1	1.5
Cryptococcus antigen	1	1
Dimorphic serology	3	6
Farmer's Lung antibodies	5	6.7
Flucytosine assay	1	1.2
Itraconazole assay	3	3.1
Mould antifungal susceptibilities	5	9.6
Mould identification	1	5
PCR (Diagnostic)	3	5
Posaconazole assay	2	2.6
Voriconazole assay	1	1
Yeast antifungal susceptibilities	2	5.5
Yeast identification	2	5

How to make the best use of our service

Please use and complete fully the standard request forms, available on the PHE web site under the heading above.

- Form Y1: Mycology Identification/Susceptibility testing.
- Form Y2: Diagnostic Mycology and Assays.

All samples should be securely packaged conforming to current postal regulations.

Cultures for identification and susceptibility testing

- Please send pure cultures on slopes rather than plates.
- For Hazard Group 3 pathogens please give the MRL advanced warning by telephone that a culture is about to be submitted. Only send slopes of cultures and do not wait for the organisms to start to sporulate.

Serological tests:

- For serological tests please supply 1-2 mL of serum (do not send whole blood).
- Samples for Beta 1-3 Glucan determination should be sent to the MRL within 48 hours of collection, preferably on ice.

Antifungal assays:

- Please contact the laboratory before submitting samples for amphotericin B or fluconazole assays, as their measurement is not often indicated.
- Please supply 1-2 mL serum taken at the appropriate times and labelled accordingly.

Guidelines for antifungal drug monitoring:

Oral flucytosine	pre-dose and 2 hours post-dose
IV flucytosine	pre-dose and 30 mins. post-dose
Oral or IV itraconazole	pre-dose after 7 days
Oral posaconazole	pre-dose after 5 days
Oral voriconazole	pre-dose after 3-5 days
IV voriconazole	pre-dose after 3-5 days
Amphotericin	1-2 hours post-dose
Oral fluconazole	2 hours post-dose
IV fluconazole	30 mins. post-dose

Please ensure all high risk samples are clearly labelled

Interpretation of Assay Results

FLUCYTOSINE

- Serum samples should be taken just before a dose of flucytosine, and 2 hours after an oral dose or 30 min after an intravenous dose. The dose and interval should be adjusted in order to produce peak serum concentrations of about 50-100 mg/L and trough concentrations of 20-40 mg/L. Levels >100 mg/L are toxic.

ITRACONAZOLE

- The trough level should be maintained above 0.5 mg/L.
- Less than 0.5mg/L is a low concentration.
- There may be toxicity issues at higher concentrations (>4 mg/L). Liver function tests should be monitored during prolonged courses.

POSACONAZOLE

- The absorption and metabolism of posaconazole will vary from patient to patient. Recommended trough concentrations are: 0.7 mg/L for prophylaxis and >1.0 mg/L for invasive disease.

VORICONAZOLE

- The absorption and metabolism of voriconazole will vary from patient to patient. The voriconazole trough concentration should be maintained above 1.0 mg/L. Outcomes for bulky or disseminated infections are better when levels are >2.0 mg/L.
- Levels above 6.0 mg/L are more likely to lead to liver toxicity and levels above 10.0 mg/L should be avoided.

AMPHOTERICIN B

- Monitoring of blood concentrations of amphotericin B, during treatment, is seldom indicated. The optimum serum concentrations of the drug for particular fungal infections have not been determined. Toxicity is assessed by monitoring renal function. Although amphotericin B is nephrotoxic, high blood concentrations do not lead to greater impairment of renal function, nor does renal failure result in higher blood concentrations.

Training Courses

The MRL organises regular training courses on the identification of pathogenic fungi. These are held at the University of Bristol and can accommodate up to 50 participants. Full details are available on request.

Individual training can be provided for NHS and PHE medical, technical and scientific staff. Please telephone or write to discuss your requirements.

External Quality Assurance

The MRL collaborates with the Quality Assurance Laboratory in organising the UK National External Quality Assurance Schemes (NEQAS) in mycology.

The laboratory itself participates in three UK NEQAS schemes; two for antibiotic assays (flucytosine & azole drugs) and the other for immunology and immunochemistry (*Aspergillus*, *Candida*, avian allergens and farmer's lung antibody tests). The MRL also takes part in external quality assurance schemes for the validation of *Aspergillus* antigen detection and fungal PCR (Quality Control for Molecular Diagnostics), as well as the Instand e.V. (Germany) Mycology External Quality Control

scheme for mould and yeast identification, cryptococcal antigen and candida antibody detection.

National Collection of Pathogenic Fungi (NCPF) (www.hpacultures.org.uk/ncpf)

The MRL is part of the Biological Resource Centre of the PHE. It houses the only UK microbial culture collection specialising in fungi pathogenic to humans and animals. At present the collection holds about 4,000 strains, many of which are available for distribution. These include:

- Approximately 700 strains of dermatophytes and related organisms from the UK and abroad from human and animal infections including many original type strains.
- Approximately 1,500 mould strains from sub-cutaneous and deep-seated human and animal infections.
- Approximately 1,500 pathogenic yeast strains.
- More than 250 strains of dimorphic fungal pathogens.

Fungal Isolates

NCPF strains are supplied for research, quality control of microbiological media, disinfectants and antifungal susceptibility tests. Current prices and conditions of sale are available on request.

DNA Services

As part of an ongoing modernisation of the collection, genomic DNA is being extracted for all of the fungal cultures in the collection. These can be made available on request.

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