Acknowledgments

UK Standards for Microbiology Investigations (SMIs) are developed under the auspices of Public Health England (PHE) working in partnership with the National Health Service (NHS), Public Health Wales and with the professional organisations whose logos are displayed below and listed on the website https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories. SMIs are developed, reviewed and revised by various working groups which are overseen by a steering committee (see https://www.gov.uk/government/groups/standards-for-microbiology-investigations-steering-committee).

The contributions of many individuals in clinical, specialist and reference laboratories who have provided information and comments during the development of this document are acknowledged. We are grateful to the medical editors for editing the medical content.

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Logos correct at time of publishing.
### Amendment table

Each SMI method has an individual record of amendments. The current amendments are listed on this page. The amendment history is available from standards@phe.gov.uk.

New or revised documents should be controlled within the laboratory in accordance with the local quality management system.

<table>
<thead>
<tr>
<th>Amendment no/date.</th>
<th>3/12.10.15</th>
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<td>1.2</td>
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<tr>
<td>Insert issue no.</td>
<td>2</td>
</tr>
<tr>
<td><strong>Section(s) involved</strong></td>
<td><strong>Amendment</strong></td>
</tr>
<tr>
<td>Page 2.</td>
<td>Updated logos added.</td>
</tr>
<tr>
<td>Scope.</td>
<td>Text updated for clarity.</td>
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</tbody>
</table>
| Introduction. | Reorganised for clarity.  
Rapid methods section added. |
| Technical information/limitations. | Addition of section on anticoagulants. |
| Safety considerations. | Reviewed and updated.  
If Hazard Group 3 organisms are not suspected, consider processing under Containment Level 2 conditions.  
Information added regarding thermally dimorphic fungi. |
| Specimen collection. | Use of blood culture bottles recommended.  
Additional specimens for direct culture, microscopy and molecular techniques should be collected in appropriate CE marked leak proof containers. |
| Specimen processing/procedure. | Addition of direct culture and molecular techniques.  
Section 4.5.1 culture media, conditions and organisms updated.  
Incubate blood culture broths for 5 days.  
Incubate FAA for 5 days.  
Incubate Sabouraud agar for 14 days. |
| Reporting procedure. | Addition of reporting for molecular methods. |
| Appendix 1. | Updated in line with section 4.5.1. |
UK SMI#: scope and purpose

Users of SMIs
Primarily, SMIs are intended as a general resource for practising professionals operating in the field of laboratory medicine and infection specialties in the UK. SMIs also provide clinicians with information about the available test repertoire and the standard of laboratory services they should expect for the investigation of infection in their patients, as well as providing information that aids the electronic ordering of appropriate tests. The documents also provide commissioners of healthcare services with the appropriateness and standard of microbiology investigations they should be seeking as part of the clinical and public health care package for their population.

Background to SMIs
SMIs comprise a collection of recommended algorithms and procedures covering all stages of the investigative process in microbiology from the pre-analytical (clinical syndrome) stage to the analytical (laboratory testing) and post analytical (result interpretation and reporting) stages. Syndromic algorithms are supported by more detailed documents containing advice on the investigation of specific diseases and infections. Guidance notes cover the clinical background, differential diagnosis, and appropriate investigation of particular clinical conditions. Quality guidance notes describe laboratory processes which underpin quality, for example assay validation.

Standardisation of the diagnostic process through the application of SMIs helps to assure the equivalence of investigation strategies in different laboratories across the UK and is essential for public health surveillance, research and development activities.

Equal partnership working
SMIs are developed in equal partnership with PHE, NHS, Royal College of Pathologists and professional societies. The list of participating societies may be found at https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories. Inclusion of a logo in an SMI indicates participation of the society in equal partnership and support for the objectives and process of preparing SMIs. Nominees of professional societies are members of the Steering Committee and working groups which develop SMIs. The views of nominees cannot be rigorously representative of the members of their nominating organisations nor the corporate views of their organisations. Nominees act as a conduit for two way reporting and dialogue. Representative views are sought through the consultation process. SMIs are developed, reviewed and updated through a wide consultation process.

Quality assurance
NICE has accredited the process used by the SMI working groups to produce SMIs. The accreditation is applicable to all guidance produced since October 2009. The process for the development of SMIs is certified to ISO 9001:2008. SMIs represent a good standard of practice to which all clinical and public health microbiology

Microbiology is used as a generic term to include the two GMC-recognised specialties of Medical Microbiology (which includes Bacteriology, Mycology and Parasitology) and Medical Virology.
laboratories in the UK are expected to work. SMIIs are NICE accredited and represent neither minimum standards of practice nor the highest level of complex laboratory investigation possible. In using SMIIs, laboratories should take account of local requirements and undertake additional investigations where appropriate. SMIIs help laboratories to meet accreditation requirements by promoting high quality practices which are auditable. SMIIs also provide a reference point for method development. The performance of SMIIs depends on competent staff and appropriate quality reagents and equipment. Laboratories should ensure that all commercial and in-house tests have been validated and shown to be fit for purpose. Laboratories should participate in external quality assessment schemes and undertake relevant internal quality control procedures.

**Patient and public involvement**

The SMI working groups are committed to patient and public involvement in the development of SMIIs. By involving the public, health professionals, scientists and voluntary organisations the resulting SMI will be robust and meet the needs of the user. An opportunity is given to members of the public to contribute to consultations through our open access website.

**Information governance and equality**

PHE is a Caldicott compliant organisation. It seeks to take every possible precaution to prevent unauthorised disclosure of patient details and to ensure that patient-related records are kept under secure conditions. The development of SMIIs is subject to PHE Equality objectives [https://www.gov.uk/government/organisations/public-health-england/about/equality-and-diversity](https://www.gov.uk/government/organisations/public-health-england/about/equality-and-diversity).

The SMI working groups are committed to achieving the equality objectives by effective consultation with members of the public, partners, stakeholders and specialist interest groups.

**Legal statement**

While every care has been taken in the preparation of SMIIs, PHE and any supporting organisation, shall, to the greatest extent possible under any applicable law, exclude liability for all losses, costs, claims, damages or expenses arising out of or connected with the use of an SMI or any information contained therein. If alterations are made to an SMI, it must be made clear where and by whom such changes have been made.

The evidence base and microbial taxonomy for the SMI is as complete as possible at the time of issue. Any omissions and new material will be considered at the next review. These standards can only be superseded by revisions of the standard, legislative action, or by NICE accredited guidance.

SMIIs are Crown copyright which should be acknowledged where appropriate.

**Suggested citation for this document**

Scope of document

Type of specimen
Bone marrow

This SMI describes the processing and microbiological investigation of bone marrow samples submitted for clinical diagnostic purposes. Techniques covered by this SMI include culture of bone marrow for the identification of bacteria and fungi, as well as molecular methods and rapid techniques. Other methods of investigation are available for the identification of parasites and viruses, but are not covered in this SMI.

For the investigation of bone marrow for *Mycobacterium* species refer to B 40 – *Investigation of specimens for Mycobacterium species*.

This SMI should be used in conjunction with other SMIs.

Introduction

Microbiological examination of bone marrow is an invasive technique infrequently performed for the investigation of pyrexia of unknown origin (PUO) and occasionally for other indications1. It is sometimes undertaken when other less invasive investigations and diagnostic imaging have failed to determine a cause, or, more frequently, when infection is part of the differential diagnosis in the investigation of haematological abnormalities2. The demonstration of microorganisms in bone marrow by microscopy, culture or nucleic acid amplification techniques is useful for diagnosis of infection with a limited number of bacteria, fungi, parasites and viruses3-5.

Bone marrow is aspirated from the posterior iliac crest or the sternum; a core biopsy may also be collected, and this can be examined histologically for evidence of granulomata and microorganisms. The aspirate is however the preferred specimen for microbiological studies.

Infection in patients who are immunocompromised

It has been suggested that bone marrow cultures should not be used for immunocompetent patients, but should be reserved for patients who are severely immunosuppressed6. Conditions leading to significant immunosuppression such as advanced HIV infection, bone marrow or solid organ transplant, or high dose corticosteroid therapy predispose patients to infection with opportunistic pathogens and make disseminated infection with pathogens more likely7. In these cases culture of bone marrow may be useful in the investigation of pyrexia of unknown origin (PUO)2,8-10. *Mycobacterium* species, *Histoplasma capsulatum*, *Paracoccidioides brasiliensis*, *Talaromyces marneffei* (formerly *Penicillium marneffei*) and *Leishmania* species are likely to cause disseminated infection in the setting of immunosuppression6,11.

Organisms which have been demonstrated in bone marrow

Some organisms invade bone marrow as part of a multi-system infection, whereas others have a tropism for bone marrow or the cell lines therein. In several studies, culture of bone marrow has been shown to be a faster and more sensitive method of isolation of certain organisms (for example *Brucella* species and *Salmonella* Typhi) compared to blood culture. However, in some studies similar yields and turnaround
Investigation of bone marrow

Bone marrow examination is most likely to be performed for the organisms below. The list is not exhaustive; other organisms may be detected or isolated.

**Bacteria**

**Salmonella Typhi and Salmonella Paratyphi**

*Salmonella Typhi* and *Salmonella Paratyphi* (groups A, B, and C) are the causative organisms of enteric (typhoid) fever and are usually carried by humans, and transmitted via contaminated food or water. Enteric fever is the only bacterial infection for which bone marrow is routinely recommended. Culture of bone marrow is considered to be the ‘gold standard’ method for diagnosis of typhoid fever. Blood culture may lack sensitivity and culture of bone marrow aspirates has been shown to produce a higher yield even when following antimicrobial treatment. In one study it was shown that 1mL of bone marrow gave an equivalent result to 15mL of blood. Serology is available, but has low sensitivity and specificity due to cross reactions with other *Salmonella* species and Enterobacteriaceae. Nucleic acid amplification tests (NAATs) on culture positive bone marrow aspirates have been reported, but are not yet in routine use. Cultures of *S. Typhi* and of *S. Paratyphi* A, B or C (known or suspected) must be handled at Containment Level 3.

**Brucella species**

Brucella is a zoonotic disease which has a wide range of symptoms and is thought to be greatly under diagnosed. Laboratory diagnostic techniques include culture, NAATs and antibody detection (the presence of antibodies is not always indicative of active brucellosis). Recovery from blood is suboptimal and it has been suggested that culture of bone marrow (as well as liver tissue and lymph nodes) may improve the recovery rate within a shorter time frame.

**Mycobacterium species**

*Mycobacterium* species are considered an important cause of pyrexia of unknown origin. Tuberculosis is primarily caused by *Mycobacterium tuberculosis*. A number of non-tuberculous mycobacterial species have been isolated from systemic infections in patients who are HIV positive. Culture is considered the ‘gold standard’ method for laboratory diagnosis, however incubation times may be long. The use of continuous blood culturing systems reduces culture time; positive results may be available within five to seven days. Bone marrow culture assists in aiding diagnosis in uncertain cases of disseminated disease, particularly in those with HIV. Molecular methods for detection are currently under development (refer to B 40 – Investigation of specimens for *Mycobacterium* species).

**Fungi**

Infection with dimorphic fungi such as *Histoplasma capsulatum*, *Paracoccidioides brasiliensis* or *Talaromyces marneffei* (formerly *Penicillium marneffei*) may occasionally be diagnosed by bone marrow examination, but culture sensitivity varies. Culture for *Histoplasma capsulatum* and *Paracoccidioides brasiliensis* may take between two and six weeks; continuous monitoring blood culture systems have been shown to reduce culture time of *Talaromyces marneffei* to about four days. It
has been suggested that culture of bone marrow samples may be more sensitive than other tests; however, diagnosis is more frequently made by detection of these organisms in respiratory and tissue specimens.

**Parasites**

*Leishmania* species

There are over 20 species of the protozoan parasite *Leishmania*. Humans are infected by the bite of infected female sandflies. The disease is endemic in five continents and over eighty countries. Leishmaniasis presents as three distinct syndromes, visceral (also known as Kala-azar), cutaneous and mucosal. Visceral Leishmaniasis, for which bone marrow investigation may be performed, can be fatal if untreated and is characterised by fever, weight loss, hepatosplenomegaly and pancytopenia. Co-infection with HIV in endemic areas is associated with a more rapid progression to AIDS and infection has been transmitted through needle-sharing by infected drug users in south west Europe.

Following presumptive identification using Giemsa stain to detect amastigotes, samples should be sent to the reference laboratory for confirmation. Rapid diagnostic tests including direct agglutination and immunochromographic tests (ICT) have been developed and evaluated. Serological diagnosis is available but it is significantly less sensitive in those with advanced HIV coinfection than for HIV negative individuals. Negative results should not therefore be used to rule out a diagnosis in those with HIV. Cross-reactions can occur in patients with prior exposure to *Trypanosoma cruzi*. Splenic puncture is the most sensitive test, but bone marrow examination is safer and has a sensitivity of around 70 – 80%.

**Viruses**

Many viruses can be detected in bone marrow samples. Viral detection indicates infection, but does not necessarily confirm diagnosis of disease. The clinical significance of a positive bone marrow result is dependent on the immune status of the patient and the disease/illness under investigation; positive results from bone marrow samples must therefore be interpreted with caution. Routinely, NAATs or serology on peripheral blood is used for diagnosis of acute viral infection. In the immunocompromised, blood serology results may be negative at the onset of clinical disease. If there is a high clinical suspicion of viral infection, but peripheral blood NAATs results are negative, diagnosis may be confirmed by bone marrow examination.

**Rapid techniques**

**Molecular methods**

NAAT - Nucleic Acid Amplification Techniques (eg PCR) for the identification of bacteria, fungi, parasites and viruses from clinical samples have been shown to be highly specific and sensitive. PCR targets conserved genes of the genome, and enables the rapid identification of organisms including those that are slow to grow or are unculturable. Results are available within a short timeframe particularly if multiplex real-time PCR is used.
MALDI-TOF mass spectrometry

Recent developments in identification of bacteria and yeast include the use of 16s ribosomal protein profiles obtained by Matrix Assisted Laser Desorption Ionisation – Time of Flight (MALDI-TOF) mass spectrometry. Mass peaks achieved by the test strains are compared to those of known reference strains. It is possible for an organism to be identified from an isolate within a short time frame and it is increasingly being used in laboratories to provide a robust, rapid and effective identification system for bacterial and yeast isolates.

Technical information/limitations

Limitations of UK SMIs

The recommendations made in UK SMIs are based on evidence (eg sensitivity and specificity) where available, expert opinion and pragmatism, with consideration also being given to available resources. Laboratories should take account of local requirements and undertake additional investigations where appropriate. Prior to use, laboratories should ensure that all commercial and in-house tests have been validated and are fit for purpose.

Specimen containers

SMIs use the term “CE marked leak proof container” to describe containers bearing the CE marking used for the collection and transport of clinical specimens. The requirements for specimen containers are given in the EU in vitro Diagnostic Medical Devices Directive (98/79/EC Annex 1 B 2.1) which states: “The design must allow easy handling and, where necessary, reduce as far as possible contamination of and leakage from, the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen. The manufacturing processes must be appropriate for these purposes”.

Anticoagulants

Specimens for direct culture, microscopy and molecular techniques should be collected in appropriate CE marked leak-proof containers. Various tubes containing anticoagulants may be used, manufacturer’s instructions should be consulted prior to use.

Specimens for direct culture and microscopy may be submitted in a plain sterile tube, or a sterile heparinised tube. Specimens for NAAT may be submitted in sterile tubes containing heparin or EDTA.
1 Safety considerations

1.1 Specimen collection transport and storage

Use aseptic technique.

Ideally, specimens for culture should be collected directly into blood culture bottles and transported in sealed plastic bags.

Additional bone marrow specimens should be submitted in an appropriate CE marked leak-proof containers and transported in sealed plastic bags.

Compliance with postal, transport and storage regulations is essential.

1.2 Specimen processing

Where Hazard Group 3 organisms (e.g., Mycobacterium tuberculosis, Salmonella Typhi, Salmonella Paratyphi, dimorphic fungi, and Brucella species) are suspected, all specimens must be processed in a microbiological safety cabinet under full Containment Level 3 conditions.

If Hazard Group 3 organisms are not suspected, consider processing under Containment Level 2 conditions.

All laboratory procedures (including the examination of plates and cultures) must be conducted in a microbiological safety cabinet.

Some Hazard Group 3 fungi are thermally dimorphic, and will grow as yeast form in blood culture bottles and sub-cultures at 37°C, but as the highly infective mould form when sub-cultured onto agar plates incubated at 28-30°C. Care should be taken with yeast isolates if there is a relevant travel history, especially in HIV-infected individuals.

If blood culture bottles are employed to provide an enrichment broth then any consequential use and subsequent disposal of syringes and needles must comply with local safety protocols.

Specimen containers must also be placed in a suitable holder.

Refer to current guidance on the safe handling of all organisms documented in this SMI.

The above guidance should be supplemented with local COSHH and risk assessments.

2 Specimen collection

2.1 Type of specimens

Bone marrow, bone marrow sample inoculated in a blood culture bottle

2.2 Optimal time and method of collection

For safety considerations refer to Section 1.1.

Collect specimens before starting antimicrobial therapy where possible.

Specimens for culture should ideally be collected in blood culture bottles.
Additional specimens for direct culture, microscopy and molecular techniques should be collected in appropriate CE marked leak-proof containers. For information regarding appropriate use of anticoagulants refer to technical information/limitations.

2.3 Adequate quantity and appropriate number of specimens

As large a sample as possible should be obtained, with the caveat that volumes of >3mL are likely to be contaminated with peripheral blood which may have a dilution effect.

Numbers and frequency of specimens collected are dependent on clinical condition of patient.

3 Specimen transport and storage

3.1 Optimal transport and storage conditions

For safety considerations refer to Section 1.1.

Specimens should be transported and processed as soon as possible.

4 Specimen processing/procedure

4.1 Test selection

Select a representative portion of specimen for appropriate procedures such as culture for *Mycobacterium* species.

Refer to B 40 – Investigation of specimens for *Mycobacterium* species.

4.2 Appearance

N/A

4.3 Sample preparation

4.3.1 Pre-treatment

Standard

If not already done, inoculate blood culture bottles with specimen and load onto the automated continuous monitoring blood culture system. Subculture positive bottles as required (see B 37 – Investigation of blood cultures (for organisms other than *Mycobacterium* species)).

Optional

N/A

4.3.2 Specimen processing

Standard

Bottles that flag as positive on the automated system should be subcultured according to the same procedure as for blood culture bottles (see B 37 – Investigation of blood cultures (for organisms other than *Mycobacterium* species)).
Optional
Specimens collected into appropriate CE marked leak proof containers should be used for microscopy and may be used for the following tests:

Direct culture
Where clinically indicated, direct plate culture may be required. Refer to section 4.5.

Molecular techniques
Specimens for molecular testing should be processed according to manufacturer’s instructions.

4.4 Microscopy

4.4.1 Standard

Giemsa stain
Giemsa stains should be carried out for Leishmaniasis as indicated by local protocols; a smear maybe made at the patient’s bedside or at the receiving laboratory.
Refer to TP 39 – Staining procedures

4.4.2 Optional

Gram stain
Refer to TP 39 – Staining procedures

4.4.3 Supplementary
See B 40 - Investigation of specimens for Mycobacterium species, and TP 39 - Staining procedures

4.5 Culture and investigation
Inoculate each agar plate using a sterile pipette (Q 5 - Inoculation of culture media for bacteriology).

For the isolation of individual colonies, spread inoculum with a sterile loop.
### 4.5.1 Culture media, conditions and organisms

<table>
<thead>
<tr>
<th>Clinical details/conditions</th>
<th>Specimen</th>
<th>Standard media</th>
<th>Incubation</th>
<th>Cultures read</th>
<th>Target organism(s)</th>
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</thead>
<tbody>
<tr>
<td>All clinical conditions</td>
<td>Bone marrow</td>
<td>Blood culture broths (aerobic and anaerobic)</td>
<td>35 – 37°C, Air, 5 d + terminal subculture</td>
<td>Continuous monitoring</td>
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<td>Subculture plates</td>
<td>Bone marrow</td>
<td>Blood agar</td>
<td>35 – 37°C, 5 – 10% CO₂, 40 – 48hr ≥40hr</td>
<td>Any organism</td>
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<td></td>
<td>Chocolate agar</td>
<td>35 – 37°C, 5 – 10% CO₂, 40 – 48hr* ≥40hr</td>
<td>Any organism</td>
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<td></td>
<td>FAA</td>
<td>35–37°C, Anaerobic, 5 d, 3 d and 5 d</td>
<td>Anaerobes</td>
<td></td>
</tr>
</tbody>
</table>

For these situations, add the following:

<table>
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<th>Clinical details/conditions</th>
<th>Specimen</th>
<th>Supplementary media</th>
<th>Incubation</th>
<th>Cultures read</th>
<th>Target organism(s)</th>
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</thead>
<tbody>
<tr>
<td>Systemic fungal infection</td>
<td>Bone marrow</td>
<td>Sabouraud agar (slopes)</td>
<td>28 - 30°C, Air, 14 d</td>
<td>Daily</td>
<td>Yeast and Mould</td>
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<td>Where clinically indicated</td>
<td>Bone marrow</td>
<td>Direct Culture: Blood agar</td>
<td>35 – 37°C, 5 – 10% CO₂, 40 – 48hr ≥40hr</td>
<td>Any organism</td>
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<tr>
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<td></td>
<td>Chocolate agar</td>
<td>35 – 37°C, 5 – 10% CO₂, 40 – 48hr* ≥40hr</td>
<td>Any organism</td>
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<tr>
<td></td>
<td></td>
<td>FAA</td>
<td>35-37°C, Anaerobic, 5 d, 3 d and 5 d</td>
<td>Anaerobes</td>
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</table>

Optional Molecular Techniques

<table>
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<th>Clinical details/conditions</th>
<th>Specimen</th>
<th>Molecular Technique</th>
<th>Instructions</th>
<th>Target organism(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All clinical conditions</td>
<td>Bone marrow</td>
<td>NAAT</td>
<td>Follow manufacturer’s instructions</td>
<td>Any organism</td>
</tr>
</tbody>
</table>

Other organisms for consideration: Mycobacterium species (see B 40 - Investigation of specimens for Mycobacterium species), fungi, parasites (see B 31 - Investigation of specimens other than blood for parasites), and viruses (see https://www.gov.uk/government/collections/standards-for-microbiology-investigations-smi#virology).

*Incubation times may be increased up to 5 days if Brucella species infection is suspected.
4.6 Identification
Refer to individual SMIs for organism identification.

4.6.1 Minimum level of identification in the laboratory
All organisms to species level.
Organisms may be further identified if this is clinically or epidemiologically indicated.
Note: Any organism considered to be a contaminant may not require identification to species level.

4.7 Antimicrobial susceptibility testing
Refer to British Society for Antimicrobial Chemotherapy (BSAC) and/or EUCAST guidelines.

4.8 Referral for outbreak investigations
N/A

4.9 Referral to reference laboratories
For information on the tests offered, turnaround times, transport procedure and the other requirements of the reference laboratory click here for user manuals and request forms.
Organisms with unusual or unexpected resistance, or associated with a laboratory or clinical problem, or anomaly that requires elucidation should be sent to the appropriate reference laboratory.
Contact appropriate devolved national reference laboratory for information on the tests available, turnaround times, transport procedure and any other requirements for sample submission:
England and Wales
Scotland
Northern Ireland
http://www.publichealth.hscni.net/directorate-public-health/health-protection

5 Reporting procedure

5.1 Microscopy

5.1.1 Standard
Giemsa stain
Report as indicated by local protocols.
5.1.2 Optional
Gram stain
Report organism detected.

Supplementary
For the reporting of microscopy for *Mycobacterium* species refer to B 40 – *Investigation of specimens for Mycobacterium species*.

5.1.3 Microscopy reporting time
All results should be issued to the requesting clinician as soon as they become available, unless specific alternative arrangements have been made with the requestors.

Urgent results should be telephoned or transmitted electronically in accordance with local policies.

5.2 Culture
Following results should be reported:
- clinically significant organisms isolated
- other growth
- absence of growth

5.2.1 Culture reporting time
Interim or preliminary results should be issued on detection of potentially clinically significant isolates as soon as growth is detected, unless specific alternative arrangements have been made with the requestors.

Urgent results should be telephoned or transmitted electronically in accordance with local policies.

Final written or computer generated reports should follow preliminary and verbal reports as soon as possible.

5.3 Molecular
Report results as per manufacturer’s instructions.

5.4 Antimicrobial susceptibility testing
Report susceptibilities as clinically indicated. Prudent use of antimicrobials according to local and national protocols is recommended.

6 Notification to PHE\textsuperscript{53,54}, or equivalent in the devolved administrations\textsuperscript{55-58}

The Health Protection (Notification) regulations 2010 require diagnostic laboratories to notify Public Health England (PHE) when they identify the causative agents that are listed in Schedule 2 of the Regulations. Notifications must be provided in writing, on paper or electronically, within seven days. Urgent cases should be notified orally and
as soon as possible, recommended within 24 hours. These should be followed up by written notification within seven days.

For the purposes of the Notification Regulations, the recipient of laboratory notifications is the local PHE Health Protection Team. If a case has already been notified by a registered medical practitioner, the diagnostic laboratory is still required to notify the case if they identify any evidence of an infection caused by a notifiable causative agent.

Notification under the Health Protection (Notification) Regulations 2010 does not replace voluntary reporting to PHE. The vast majority of NHS laboratories voluntarily report a wide range of laboratory diagnoses of causative agents to PHE and many PHE Health protection Teams have agreements with local laboratories for urgent reporting of some infections. This should continue.

**Note:** The Health Protection Legislation Guidance (2010) includes reporting of Human Immunodeficiency Virus (HIV) & Sexually Transmitted Infections (STIs), Healthcare Associated Infections (HCAIs) and Creutzfeldt–Jakob disease (CJD) under ‘Notification Duties of Registered Medical Practitioners’: it is not noted under ‘Notification Duties of Diagnostic Laboratories’.

https://www.gov.uk/government/organisations/public-health-england/about/our-governance#health-protection-regulations-2010

Other arrangements exist in **Scotland**[^55][^56], **Wales**[^57] and **Northern Ireland**[^58].
Appendix 1: Investigation of bone marrow by culture

Bone marrow specimen

Direct Culture: Optional

Enrichment Culture
Processed specimen - all inoculated blood culture bottles

Standard

Where clinically indicated

All clinical conditions

Supplementary

Systemic fungal infection

Blood agar

Chocolate agar

FAA

Sabouraud agar

Incubate at 35-37°C 5-10% CO₂ 40-48hr
Read at 40hr

Incubate at 35-37°C 5-10% CO₂ 40-48hr
Read at 40hr

Incubate at 35-37°C Anaerobic 5 d
Read at 3 d, and 5 d

Incubate at 28-30°C
In air
14 d
Read Daily

Any organism Refer to IDs

Any organism Refer to IDs

Anaerobes Refer to ID 8, 10, 14, 25

Yeast Mould
References


21. van Schalkwyk WA, Opie J, Novitzky N. The diagnostic utility of bone marrow biopsies performed for the investigation of fever and/or cytopenias in HIV-infected adults at Groote Schuur Hospital, Western Cape, South Africa. Int J Lab Hematol 2011;33:258-66.


34. European Parliament. UK Standards for Microbiology Investigations (SMIs) use the term "CE marked leak proof container" to describe containers bearing the CE marking used for the collection and transport of clinical specimens. The requirements for specimen containers are given in the EU in vitro Diagnostic Medical Devices Directive (98/79/EC Annex 1 B 2.1) which states: "The design must allow easy handling and, where necessary, reduce as far as possible contamination of, and leakage from, the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen. The manufacturing processes must be appropriate for these purposes".


