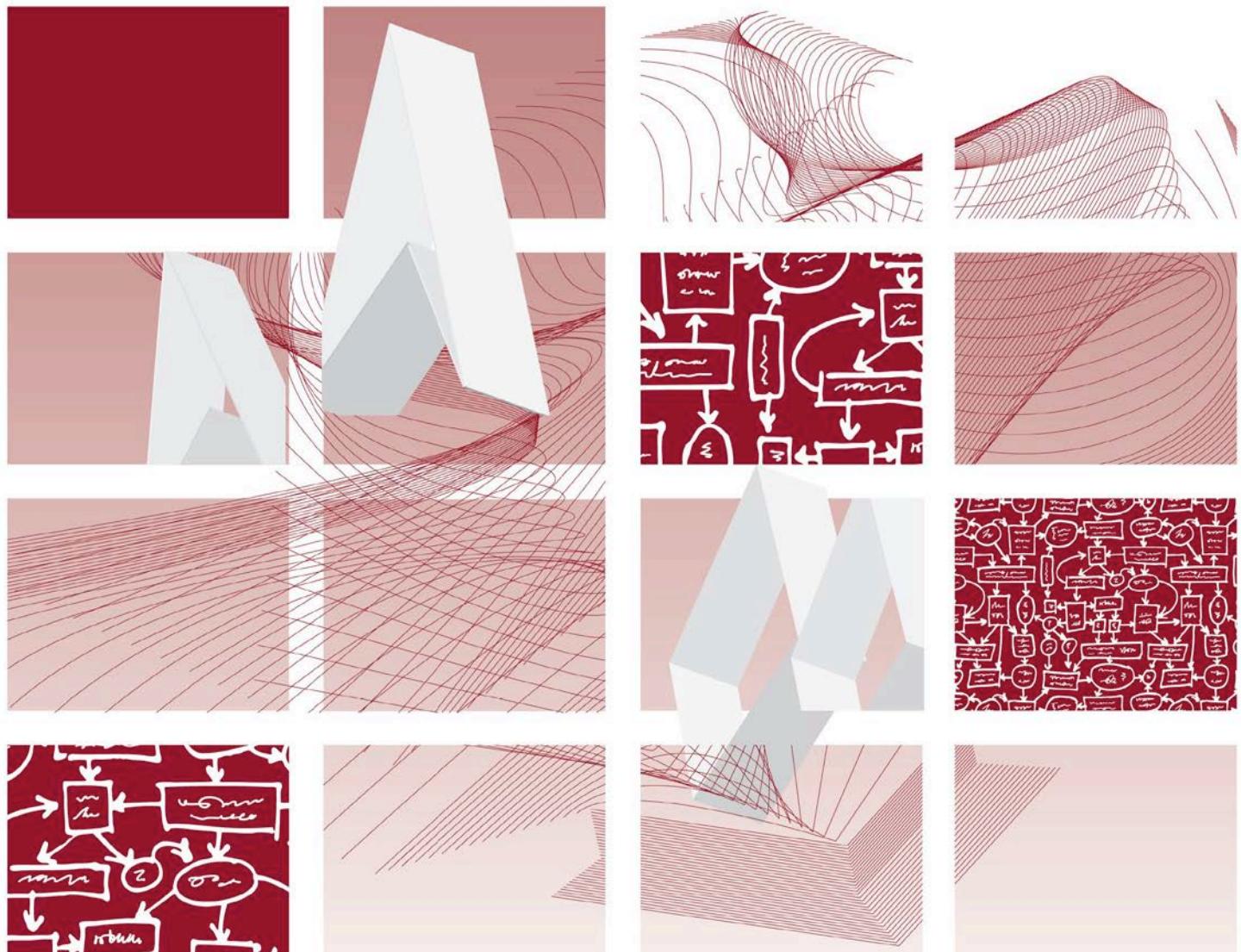




UK Standards for Microbiology Investigations

Meningoencephalitis



Issued by the Standards Unit, Microbiology Services, PHE

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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 <http://www.hpa.org.uk/SMI/Partnerships>. SMIs are developed, reviewed and revised by various working groups which are overseen by a steering committee (see <http://www.hpa.org.uk/SMI/WorkingGroups>).

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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NICE has accredited the process used by Public Health England to produce Standards for Microbiology Investigations. Accreditation is valid for 5 years from July 2011. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

For full details on our accreditation visit: www.nice.org.uk/accreditation.

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.

Amendment No/Date.	-/08.05.14
Issue no. discarded.	-
Insert Issue no.	1
Section(s) involved	Amendment

UK Standards for Microbiology Investigations[#]: Scope and Purpose

Users of SMIs

- SMIs are primarily intended as a general resource for practising professionals operating in the field of laboratory medicine and infection specialties in the UK.
- SMIs 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.
- SMIs 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 <http://www.hpa.org.uk/SMI/Partnerships>. 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.

[#]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.

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 laboratories in the UK are expected to work. SMIs are NICE accredited and represent neither minimum standards of practice nor the highest level of complex laboratory investigation possible. In using SMIs, laboratories should take account of local requirements and undertake additional investigations where appropriate. SMIs help laboratories to meet accreditation requirements by promoting high quality practices which are auditable. SMIs also provide a reference point for method development.

The performance of SMIs 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 SMIs. 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 SMIs are subject to PHE Equality objectives http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317133470313. 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

Whilst every care has been taken in the preparation of SMIs, 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.

SMIs are Crown copyright which should be acknowledged where appropriate.

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Public Health England. (2014). Meningoencephalitis.UK Standards for Microbiology Investigations. S 5 Issue 1. <http://www.hpa.org.uk/SMI/pdf>.

Scope of Document

UK Standards for Microbiology Investigations (SMIs) comprise a collection of recommended algorithms for initial test selection and testing methods and confirmatory strategies. UK SMIs also contain guidance notes that describe the recommended standard set of investigations consistent with current good practice in different infective disease presentations, as well as examples of standard laboratory practice and general information on clinical syndromes.

The syndromic algorithms form part of the pre-analytical stage of the investigative process and are intended to guide clinicians and diagnostic laboratory staff in the choice of the correct pathway for the investigation of a sample based upon the clinical context. It is recognised that clinical details are essential to the optimal processing of samples and the documents perform best when sufficient, relevant, clinical details are provided at the time of sample submission. The algorithms are presented in flowchart format to give a clear overview of how to proceed with the testing of specimens and the possible outcomes using the clinical history provided. If the primary testing set does not identify a causative pathogen, secondary testing should be performed if clinical and/or epidemiological features support such testing. Laboratories may wish to undertake second line tests either after, or at the same time as, the primary testing set according to the clinical and local epidemiological setting and laboratory operational capabilities. The flowcharts are intended to reflect current recommended practice, accounting for prevalence of infections in the UK, public health needs, and availability of tests, with references and links to more detailed guidance. National surveillance programmes for specific organisms should be taken into consideration when using the algorithms.

This document should be read in conjunction with relevant SMIs for laboratory processing and reporting of target organisms and public health actions.

S 5 – Meningoencephalitis: Scope

The intended scope of this document is to describe which infections, and relevant associated tests, should be considered according to the different clinical presentations of meningoencephalitis. [B 27 - Investigation of Cerebrospinal Fluid](#) and [G 4 - Viral Encephalitis and Meningitis](#) should be referred to for further information.

The syndromes included in this SMI have been selected to reflect the common presenting complaints of patients with meningoencephalitis. Patients who are immunocompromised may have atypical clinical features due to an altered immune response or disseminated infection.

The target organisms for bacterial meningitis include:

- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
- *Haemophilus influenzae*
- *Escherichia coli*
- *Listeria monocytogenes*
- Group B Streptococcus

The target organisms for viral meningitis and encephalitis include:

- Herpes Simplex Virus
- Varicella Zoster Virus
- Enteroviruses
- Parechovirus – only in those under three years of age

Meningitis is defined as inflammation of the meninges. This process may be acute or chronic and may result from infective or non-infective stimuli. A wide range of infective agents have been shown to cause meningitis, including viruses, bacteria, fungi and parasites.

Encephalitis is part of the spectrum of inflammatory diseases of the central nervous system, characterised by evidence of an inflammatory process involving brain parenchyma.

Encephalitis has over 100 causes, including viral infections (the majority), infection associated with other microorganisms and immune-mediated conditions (including post-infectious inflammatory processes). The time course of disease may be acute (most viral encephalitis), sub-acute, or chronic. Viral encephalitis is usually acute and is often associated with some elements of meningitis (ie meningoencephalitis), although neck stiffness occurs in less than one in three cases^{1,2}.

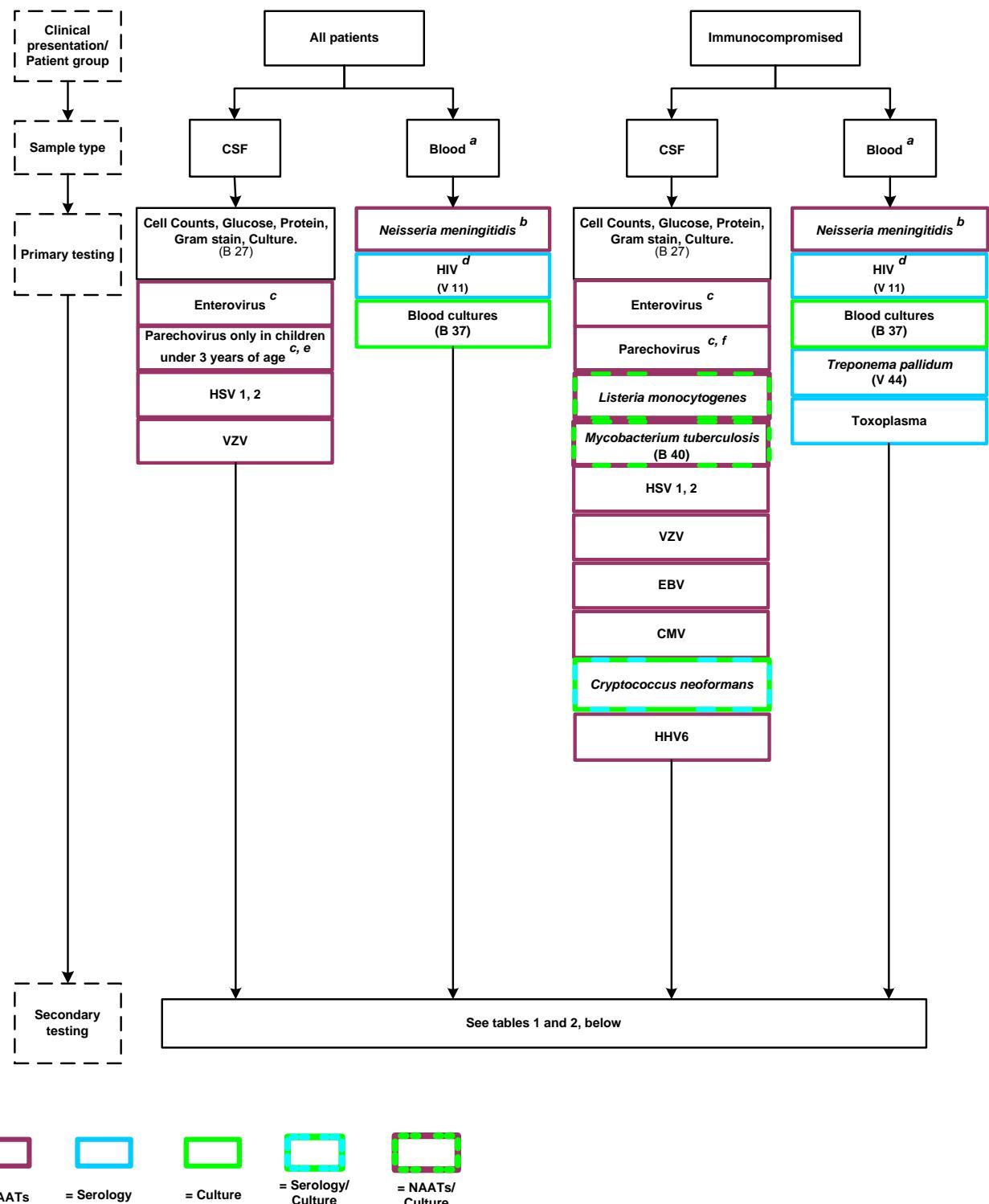
Most studies report that the aetiology of encephalitis is unclear in at least 40% of cases. A UK wide study on the Aetiology of Encephalitis found an infectious cause in 42% of cases most commonly herpes simplex virus (19%), varicella zoster virus (5%) and *Mycobacterium tuberculosis* (5%)². A further 21% of cases had acute immune-mediated encephalitis, and 37% were of unknown aetiology². Arboviruses and rabies, are common causes of meningoencephalitis in some parts of the world.

A useful case definition for encephalitis is encephalopathy (altered level of consciousness, cognition, behaviour or personality persisting for more than 24 hours) and two or more of the following²:

- Fever or history of fever ($\geq 38^{\circ}\text{C}$)
- Seizures and/or focal neurological findings
- CSF pleocytosis ($>4 \text{ WBC}/\mu\text{L}$)
- EEG findings compatible with encephalitis
- Abnormal results of neuroimaging (with evidence of brain parenchyma involvement)²

Most have fever, headache and changes to behaviour or level of consciousness. Prognosis may depend on early initiation of appropriate treatment and thus the importance of making an aetiological diagnosis cannot be overemphasized. A systematic approach should be followed for initial investigation, although clinical features, season and travel history are vital for formulating the differential diagnosis.

Meningoencephalitis¹⁻⁸



To view associated SMI documents please access from: <http://www.hpa.org.uk/SMI>

Footnotes

- a) A blood sample taken at the same time as the CSF can be helpful when interpreting the NAAT test results of CSF contaminated with blood.
- b) This should be done for suspected meningitis^{9,10}.
- c) Throat swabs and faeces are additional, appropriate, sample types for diagnosis of enteroviruses. Detection of virus in these samples is suggestive, but not diagnostic, of the cause of illness.
- d) HIV testing is recommended for all adults with meningoencephalitis. Consult guidelines for advice on testing children. In all cases a risk assessment and consideration of other features should be made¹¹.
- e) Prevalence suggests testing under the age of 3 in the immunocompetent. Testing outside of this age is not recommended. This test is not freely available in all laboratories and this may cause delay in the results^{12,13}.
- f) Immunocompromised patients can present with a wider range of pathogens, in this context HPeV should be considered in all age groups.

Table 1: Secondary testing to be considered for all patients (dependent on epidemiological factors and clinical findings)

Bacteria	Test
<i>Bartonella henselae</i>	Serology
<i>Brucellosis</i>	Serology, NAAT
<i>Chlamydophila species</i>	Serology, NAAT
<i>Coxiella burnetii</i> (Q fever)	Serology
<i>Cryptococcus neoformans</i>	Antigen detection, culture, microscopy
<i>Leptospirosis</i>	Serology, NAAT
<i>Listeria monocytogenes</i>	Blood culture, NAAT
<i>Borrelia</i> species	Serology
<i>Mycobacterium tuberculosis</i>	Microscopy, Culture, NAAT
<i>Mycoplasma species</i>	Serology, NAAT
<i>Neisseria meningitidis</i>	NAAT
<i>Streptococcus pneumoniae</i>	NAAT
<i>Treponema pallidum</i>	Serology, NAAT
Whipple's disease	NAAT
Unknown bacterial pathogen	16S PCR
Viruses	Test
Adenovirus	NAAT
CMV	NAAT
EBV	NAAT
Human Parvovirus B19	Serology, NAAT
Flaviviruses	Serology, NAAT
HHV6*	NAAT
HHV7*	NAAT
Influenza	NAAT
Lymphocytic choriomeningitis	Serology
Measles	Serology, NAAT
Mumps	Serology, NAAT
Rotavirus*	NAAT
Other	Test
Amoebae	Microscopy

<i>Aspergillus</i> species	Microscopy, galactomannan, NAAT
Antibody-associated encephalitis	Immunology

* Should be considered in children under three years of age.

Table 2: Additional testing to consider for returning travellers

Advice should be sought from a regional or national specialist in infectious disease for other possible causes of meningoencephalitis.

For more information regarding possible causes of encephalitis from foreign travel see the [British Infection Association Guidelines](#).

See the [European Federation of Neurological Societies](#).

Pathogen	Test(s)
Japanese encephalitis virus (Flavivirus)	Serology, NAAT
West Nile virus (Flavivirus)	Serology, NAAT
Tick-borne encephalitis virus (Flavivirus)	Serology, NAAT
Murray Valley encephalitis virus (Flavivirus)	Serology, NAAT
St Louis encephalitis virus (Flavivirus)	Serology, NAAT
Eastern, Western and Venezuelan equine encephalitis virus (Alphavirus)	Serology, NAAT
Chikungunya virus (Alphavirus)	Serology, NAAT
La Crosse virus (Bunyavirus)	Serology, NAAT
Colorado tick fever virus (Coltivirus)	Serology, NAAT
Nipah virus (paramyxovirus)	Serology, NAAT
Hendra virus (paramyxovirus)	Serology, NAAT
Rabies, Lyssavirus (Rhabdoviruses)	Serology, NAAT
Eosinophilic meningitis – angiostrongyliasis, gnathostomiasis, other parasites	Microscopy, Serology
<i>Trypanosoma</i> species	Microscopy, Antigen detection
Dimorphic fungi including <i>Coccidioides</i> species and <i>Histoplasma</i> species	Serology, Culture, Antigen detection
<i>Rickettsia</i> species	Serology, NAAT
Ehrlichia and Anaplasma	Serology

Notification to PHE^{14,15} or Equivalent in the Devolved Administrations¹⁶⁻¹⁹

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 (HCAs) and Creutzfeldt–Jakob disease (CJD) under ‘Notification Duties of Registered Medical Practitioners’: it is not noted under ‘Notification Duties of Diagnostic Laboratories’.

<http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/HealthProtectionRegulations/>

Other arrangements exist in [Scotland](#)^{16,20}, [Wales](#)¹⁸ and [Northern Ireland](#)¹⁹.

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