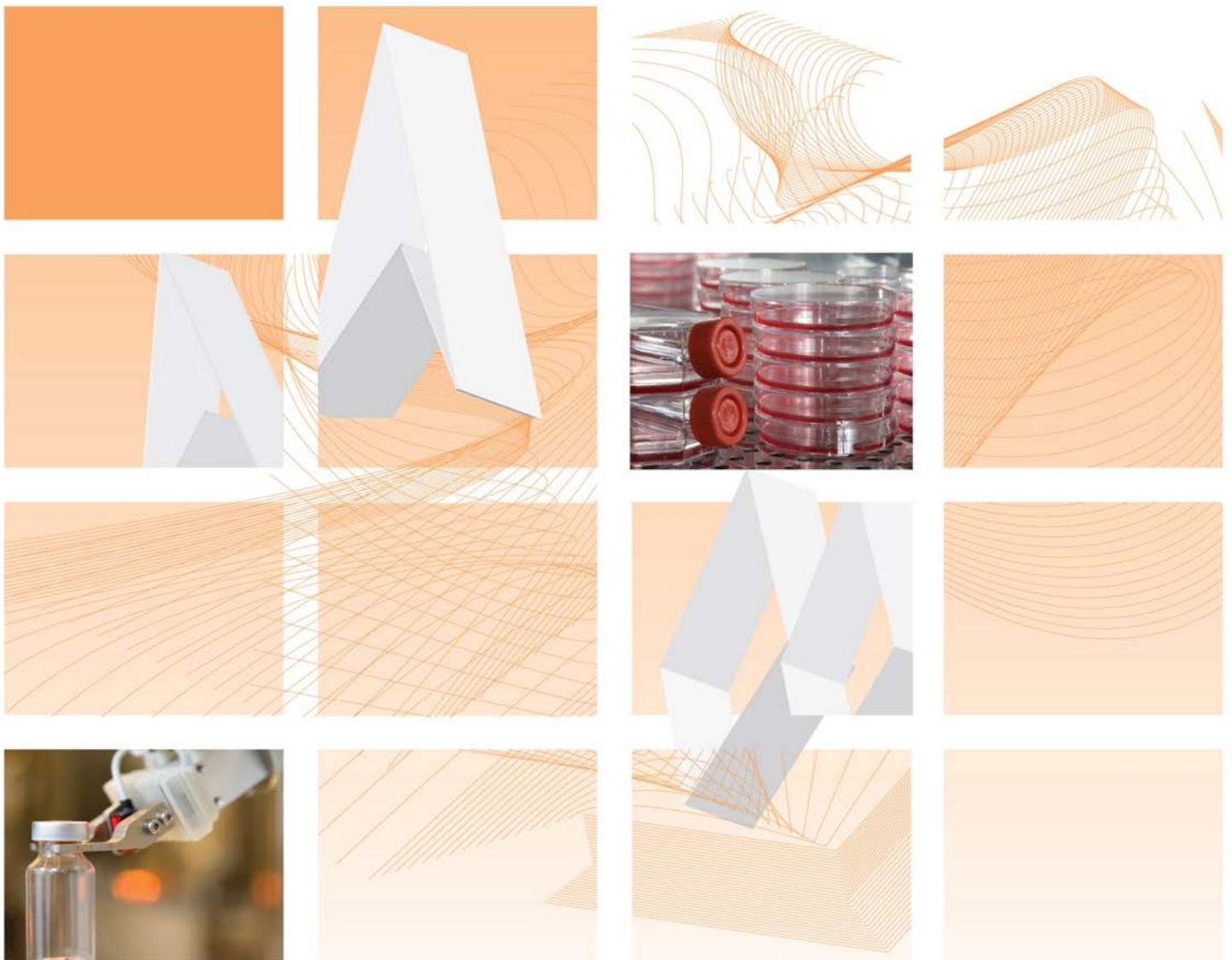




UK Standards for Microbiology Investigations

Good practice when undertaking serology assays for infectious diseases



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

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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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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.	1/12.04.16
Issue no. discarded.	1
Insert issue no.	2
Section(s) involved	Amendment
Whole document.	<p>Hyperlinks updated to gov.uk.</p> <p>Title of the document has been slightly amended.</p> <p>Section 6 of the document has been improved to include verifications.</p> <p>Reorganisation of some text.</p> <p>Professional body logos have been reviewed and updated.</p>
References.	Some references updated.

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 laboratories in the UK are expected to work. SMIs are NICE accredited and represent

[#] 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.

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 is subject to PHE equality objectives <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 SMIs, PHE and the partner organisations, 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 by an end user to an SMI for local use, it must be made clear where in the document the alterations have been made and by whom such alterations have been made and also acknowledged that PHE and the partner organisations shall bear no liability for such alterations. For the further avoidance of doubt, as SMIs have been developed for application within the UK, any application outside the UK shall be at the user's risk.

The evidence base and microbial taxonomy for the SMI is as complete as possible at the date 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.

Suggested citation for this document

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<https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories>

Scope of document

This SMI describes the essential components of a good microbial serology service. A broad definition of serology is used in this document to include both antibody and antigen tests that are performed, usually on blood samples, to detect infection, exposure or immunity.

Conventionally, microbiology and virology laboratories perform microbial serology assays. In an increasing number of laboratories some tests are performed using analysers on automated blood sciences tracks. It is important to recognise the critical pre-analytical, analytical and post-analytical steps and procedures which are essential to the delivery of a high quality service.

The principles described in this document are also relevant to nucleic acid amplification tests (NAATs) performed on blood samples, especially where microbial serology and NAATs are available for the same infection and may be listed together in order entry systems. In these circumstances there should be an experienced assessment of the appropriateness of performing serology tests or NAATs as part of a unified process that may include changing the request from a NAAT to a serology test, or vice versa. For further information on NAATs, refer to [Q 4 – Good practice when performing molecular amplification assays](#).

This SMI should be used in conjunction with other SMIs.

Introduction¹⁻⁴

Good practice in the laboratory is referred to as “a set of principles that provides a framework within which laboratory studies are planned, performed, monitored, recorded, reported and archived”⁵. Good practice in the laboratory aims to support the delivery of quality test data and to facilitate a sound approach to the management of laboratory testing, including conduct, reporting and archiving.

The delivery of a good microbial serology service is faced with a number of challenges:

- there are many serology tests and NAATs available to diagnose bacterial, viral, fungal or parasitic infections. This large choice of tests often confuses the requesting practitioner who, sometimes, has only a limited understanding of infection and of the appropriate use of these tests
- many laboratories offer electronic Order Entry to an increasing proportion of their users. In this setting, a bewildering or unfamiliar array of tests often leads to inappropriate requests. Conversely, when hand-written requests are made, considerable experience is often required to determine which tests are requested and/or are appropriate to the clinical details
- microbial serology testing can be fragmented across more than one pathology discipline (eg analysers in microbiology/virology and biochemistry)
- microbial serology results are not purely numerical results with “in-range” and “out-of-range” interpretations. The interpretation of results is complex and is an essential component of a proper microbial serology service
- it is essential that adequate training and support for interpreting results is given to staff, especially those providing point of care testing to patients⁶

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- some microbial serology results must trigger appropriate, reflex investigations, which often involves testing on different analysers or sending to reference laboratories
- follow up or retrospective testing is often of great clinical benefit. Thus, in comparison to other blood science disciplines, there is need for longer term storage of microbial serology samples

1 Ordering microbial serology tests⁶⁻⁸

Hand-written test request cards are increasingly being replaced by electronic order entry systems. While hand-written requests may not always be legible, intelligible or give clear indications of what tests are required, electronic order entry systems, with extensive test menus may encourage inappropriate or excessive requests.

All requesting systems used for microbial serology tests should:

- record who placed the order, along with the contact details
- require the entry of relevant clinical details, as this allows laboratory staff or the electronic system to allocate the most appropriate tests
- offer “syndromic order sets” in preference to individual tests whenever appropriate. This can facilitate appropriate testing and reduce the risk of missed or delayed diagnosis. Example scenarios, in which serological testing for a panel of relevant causes would normally be better practice than testing for individual infections, include: acute hepatitis; glandular fever syndrome; lymphadenopathy; or culture negative endocarditis⁹
- require the entry of the date of onset of symptoms, when applicable, to facilitate meaningful testing and interpretation
- require the entry of date(s) of exposure for testing following disease contact (eg pregnant woman exposed to rash)
- prompt the requesting practitioner to enter the geographic and temporal details of any relevant travel history

Experienced microbiology/virology staff play a critical role in setting up and maintaining safe and effective order entry systems.

2 Pre-analytical assessment of microbial serology tests⁶⁻⁸

As noted above, it is often beneficial to adhere to a syndromic testing algorithm with minimum deviation. When required, test selection for samples should also be overseen by trained and experienced staff who actively maintain competency. This task will normally be undertaken by microbiology staff, as they are more familiar with: the infection terminology provided by requesting clinicians; the extensive range of serology/NAAT tests available; and the clinical indications for these tests. The outcome of this scrutiny may be that alternative or additional tests are performed, or discussed with the requesting clinician, if the original request appears inappropriate. For example, it is not uncommon for serology tests to be performed instead of inappropriate NAATs.

Each laboratory should maintain a Standard Operating Procedure which details and underpins local practices for pre-analytical assessment, including criteria for:

- selecting “syndromic order sets”, and or reallocating individual tests requests to “syndromic order sets” when appropriate
- adding additional tests, where there is a clear indication that this would be of immediate clinical benefit

- rejecting requests: some tests will be appropriate only if specific clinical details are provided or a certain interval has elapsed from the date of onset. If it is decided not to perform the requested test, a report explaining the decision should be released, in order to allow the user to provide more information to support their request. It should be noted that laboratories can alter the tests requested if inappropriate, and perform other necessary tests at their discretion, however the clinician must be informed⁶. Other criteria which could also lead to rejection of clinical specimens for testing may be⁷:
 - unlabelled or improperly labelled specimen
 - non-sterile or leaking specimen/sample container
 - inappropriate specimen transport conditions
 - illegible or absent information on the request form
 - mismatched form and specimen
 - inappropriate specimen type
- re-allocating to a non-serological test type: for instance, requests for hepatitis NAAT from non-specialists may be submitted by mistake instead of a request for serology. It may be clinically (and financially) preferable to perform hepatitis serology testing, if experienced scrutiny of the clinical details and any previous test results supports this, as hepatitis B/C NAAT is usually appropriately requested only after a diagnosis of this infection is made based on serology tests
- involving the medical microbiologist or virologist in deciding what tests are appropriate. More clinical information, or a review of the patient, may be required. The SOP should provide details of when and how the medical microbiologist is involved. In some laboratories there are daily face to face “bench rounds” while in others, staff can refer a request electronically to the medical microbiologist

3 Analysis of specimens⁸

Analysis of the specimens should conform to the local Standard Operating Procedures (SOPs). These SOPs should reflect the UK Standards for Microbiology Investigations (SMIs) as well as guidance from other relevant national and international bodies.

Testing may take place using analysers integrated into automated track systems, free-standing analysers and/or manual assays. “Reflex testing” rules, based on algorithms established by laboratory professionals, can be set up on some systems to confirm or exclude a diagnosis suggested by the results of the initial test¹⁰.

4 Post-analytical assessment of results, reflex testing and reporting⁶

The key requirements for delivering a high quality, post-analytical microbial serology service are as follows:

- additional “reflex” and confirmatory testing should be performed on the sample, if appropriate (potentially via regional or national reference laboratories). The

SOP should specify which reflex or confirmatory tests may be required for each serology test, depending on the results obtained and in line with national and local practice guidelines⁸

- the analyser and/or reagent kit used for each test should be recorded. This may help in the interpretation of the results (as different kits/reagents can vary in performance) and provides critical information when recall notices are issued. It may also be a requirement for accreditation
- reports generated must be concise, readable, standardised in format, and presented chronologically. The test report should include the following items: patient identifiers; the name and address of the laboratory location where the test was performed; the date and time of specimen receipt into the laboratory; the date and time of the assay report; the name of the test performed; specimen type (eg blood, cerebrospinal fluid); and the test result
- suitable interpretative comments should be appended to the results, when required, to prompt the clinical user to respond in the appropriate way. Some comments will be pre-determined and routinely added to certain results. Others may be *ad-hoc* comments which take into account the clinical details for a specific sample and result^{6,8}
- significant results (for instance those suggesting a recent infection), should be verified by medical microbiology staff. Local SOPs should define which results require medical verification. The aim of verification is: to check the technical and clinical validity of the result; to check whether further tests are required on the same sample; to append *ad hoc* comments; and to recommend treatment or further follow-up investigations when clinically appropriate^{6,8}
- urgent results should be communicated rapidly to appropriate bodies (including the requestor and public health professionals). Local SOPs should define which results require urgent communication, in order to facilitate timely clinical or public health interventions (including provision of prophylaxis eg immunoglobulins)^{6,8}
- results indicating certain communicable diseases should be electronically reported to Public Health England (or the equivalent public health body in devolved administrations). It is the responsibility of the microbiology staff, working in collaboration with public health bodies, to set up and maintain an appropriate reporting mechanism. Notifiable results requiring immediate public health intervention (eg acute hepatitis A or B), should normally be telephoned to the Public Health team by the medical microbiology staff, in advance of the electronic report, together with available information about the clinical presentation and interpretation^{6,8}
- routine biochemistry and haematology samples are stored in diagnostic laboratories for only a few days; however, it is essential that there is longer storage of microbial serology samples. The duration of storage should permit relevant additional testing, or the demonstration of seroconversion, in order to obtain a diagnosis¹¹. The Infectious Diseases in Pregnancy Screening Programme Handbook for laboratories (October 2012) requires storage for a minimum of 2 years³. Safety of Blood, Tissues and Organs guidance (SaBTO) advises storage of donor blood specimens for a minimum of 10 years and 30 years for recipient material¹¹. Current storage practices for other specimens,

ranging from 2 months to 2 years, are not standardised and often depend on the local availability of freezer space. Information on the frequency and utility of retesting these specimens would be necessary in order to make a specific national recommendation on the duration of storage^{6,8}

- clinical results and reports may be archived either on or off site, however, they must be easily and readily retrievable within an appropriate time frame if needed

5 Quality assurance

Quality Assurance in microbial serology testing should be provided as outlined in the UK Standards for Microbiology Investigations Quality Guidance [Q 2 – Quality assurance in the diagnostic virology and serology laboratory](#).

Where microbial serology tests are performed on analysers integrated into blood sciences track systems, the most suitable arrangements for Quality Assurance would normally be as follows:

- responsibility for performing and monitoring Quality Control procedures (internal QCs) should be shared between the staff managing the track system (blood sciences staff) and the microbiology staff^{6,8}
- responsibility for managing Quality Assessment (EQA schemes) results, including responding to failures, should be attributed to trained microbiology staff who undertake this task on a regular basis^{6,8}

The strategic overview (including decisions on testing strategies, assessment of new testing protocols, response to poor NEQAS results and audit) would normally be conducted by senior medical and technical staff in microbiology.

6 Evaluations, validations and verification of assays⁸

All assays should undergo suitable evaluation, verification or validation before being implemented for routine use in the laboratory, in accordance with the principles laid out in [Q 1 – Evaluations, validations and verifications of diagnostic tests](#).

7 Other components of a good microbial serology service

- regular audit of serology results, in particular those that assess the accuracy and predictive value of screening tests, should be performed. Such audits, which are particularly useful for laboratories which provide only the initial screening tests for infections like HIV or hepatitis A/B/C, may look at the correlation between the numeric result obtained with the screening test and the probability of that result being confirmed by further testing. Knowledge of this probability is essential for initiating an appropriate, immediate clinical response to reactive screening tests results⁸

Good practice when undertaking serology assays for infectious diseases

- there should be appropriate and relevant information in the laboratory users' guide/handbook. This will usually be an online document and should be updated regularly⁸
- trained microbiology staff should provide strategic oversight of all microbial serology tests (including those performed on automated blood sciences tracks), respond to new national guidelines or scientific advances and assess new testing strategies in a timely fashion⁸
- microbiology staff may manage the appropriate use of specific immunoglobulins (eg VZIG, HBIG), either directly or via a collaborating pharmacy department⁸
- microbiology staff should support and attend regular meetings with users of microbial serology and NAAT tests, for example infectious diseases, antenatal services, sexual health, haematology and gastroenterology/hepatology⁸

References

Modified GRADE table used by UK SMI's when assessing references

Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) is a systematic approach to assessing references. A modified GRADE method is used in UK SMI's for appraising references for inclusion. Each reference is assessed and allocated a grade for strength of recommendation (A-D) and quality of the underlying evidence (I-VI). A summary table which defines the grade is listed below and should be used in conjunction with the reference list.

Strength of recommendation		Quality of evidence	
A	Strongly recommended	I	Evidence from randomised controlled trials
B	Recommended but other alternatives may be acceptable	II	Evidence from non-randomised studies
C	Weakly recommended: seek alternatives	III	Non-analytical studies, eg case reports, reviews, case series
D	Never recommended	IV	Expert opinion and wide acceptance as good practice but with no study evidence
		V	Required by legislation, code of practice or national standard
		VI	Letter or other

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