UK Standards for Microbiology Investigations

Good practice when ordering and undertaking diagnostic tests for infectious disease serology

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Contents

Amendment table

Each UK SMI 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.	2/04.08.21
Issue no. discarded.	2
Insert issue no.	3
Anticipated next review date*	04.08.24
Section(s) involved	**Amendment**
All	Document was previously titled “good practice when undertaking serology assays for infectious diseases”, and has been renamed “good practice when ordering and undertaking diagnostic tests for infectious disease serology”
All	Template updated, sections renumbered and references updated
3	Section 3, “analysis of specimens” has been removed
7	Section 7, “other components of a good microbiology serology service” has been removed
7.2	Reference to the Royal College of Pathologists / Institute of Biomedical Science “chain of evidence” document added

*Reviews can be extended up to five years subject to resources available.

1 General information

View general information related to UK SMIs.

2 Scientific information

View scientific information related to UK SMIs.

3 Scope of document

This UK SMI describes the essential components of a good microbial serology service. This document covers antibody and antigen tests that are performed, usually on blood samples, to detect infectious organisms or an infection-associated immune response.

Conventionally, microbial serology assays are carried out in microbiology and virology laboratories. In an increasing number of laboratories some microbial serology tests are performed using analysers on automated blood sciences tracks. When establishing a microbial serology service, in any setting, 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 the specific tests requested, guided by clinical algorithms and existing guidelines. For further information on NAATs, refer to Q 4 – Good practice when performing molecular amplification assays.

This UK SMI should be used in conjunction with other UK SMIs.

4 Introduction

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”[1]. Good practice in the laboratory aims to support the delivery of high-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:

- numerous serology tests and NAATs are available to support diagnosis or provide evidence of 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; design of this is further discussed in section 5. A poorly designed electronic order system can lead to inappropriate requests. It is crucial for

laboratory staff to be involved in order system design. Advisory statements can be utilised to guide appropriate test selection

- when handwritten requests are made, considerable experience is often required to determine which tests are requested and/or are appropriate to the clinical details
- infectious disease testing may be fragmented across more than one pathology discipline (eg analysers in microbiology/virology and biochemistry), and across multiple sites
- 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
- staff who interpret results must receive adequate training and support under local laboratory governance to ensure competency, including those staff providing point of care testing to patients[2]
- some microbial serology results must trigger appropriate, reflex investigations, which often involves testing samples on different analysers or sending samples 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

5 Ordering microbial serology tests[2,3]

Handwritten test request cards are increasingly being replaced by electronic order entry systems. While handwritten requests may not always be legible, intelligible or provide appropriate information to determine which tests are required, electronic order entry systems can also have disadvantages. For example, extensive test menus may encourage inappropriate or excessive requests, and systems or algorithm structures that are primarily designed for ordering blood sciences tests may not easily allow the microbiology laboratory to obtain and utilise sufficient clinical information to determine the tests required.

All requesting systems used for microbial serology tests should:

- ensure accurate identification of the patient and their specimen[3];
- record who placed the order, along with appropriate contact details to allow urgent/out of hours communication about the sample (if necessary);
- require the entry of relevant clinical details, as this allows laboratory staff or the electronic system to allocate the most appropriate tests. It is helpful for mandatory information to be collected and recorded in a categoric / pre-determined format (where possible), rather than as free text, to allow it to be incorporated into simple algorithms for ordering 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 endocarditis[4];

- 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;
- prompt the requesting practitioner to enter the geographic and temporal details of any relevant travel history;

Close collaboration between experienced microbiology/virology staff, IT suppliers and clinical user representatives is essential to designing, implementing and maintaining safe and effective electronic order systems.

Local user manuals should be consulted for further guidance, including on specimen collection and handling. Specimen requirements for NAATs should be discussed with the receiving laboratory as specimen types may not be interchangeable with serological specimens.

6 Pre-analytical assessment of microbial serology tests[2,3]

As noted above, for many clinical scenarios it is beneficial to follow a syndromic testing algorithm to determine the minimum testing that should be performed. When required, test selection for samples should also be overseen by trained and experienced staff (who actively maintain competency) in line with local laboratory procedures and clinical test selection protocols. 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 (SOP) which details and underpins local practices for pre-analytical assessment, including criteria for:

- selecting “syndromic order sets”, and or reallocating individual test requests to “syndromic order sets” when appropriate
- adding additional tests, where there is a clear indication that this would be of immediate clinical benefit, taking into consideration consent requirements and following discussion with the requester where appropriate
- rejecting requests: some tests will be appropriate only if specific clinical details are provided or a certain interval has (or has not) 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 may alter the tests ordered if they are deemed inappropriate to the clinical scenario, and may perform other necessary tests at their discretion, however the clinician must be informed[2]. Other criteria which could also lead to rejection of clinical specimens for testing include[3]:
    - unlabelled or improperly labelled specimen

  - non-sterile or leaking specimen/sample container
  - inappropriate specimen transport conditions (including significant delay)
  - illegible or absent information on the request form
  - mismatched form and specimen
  - inappropriate specimen type or insufficient sample volume
- re-allocating to an alternative 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. For example, hepatitis B and hepatitis C NAAT tests are usually appropriate only after a diagnosis of this infection is made based on serology tests (for further information, refer to UK SMIs V 4, V 5 and V 8).
- 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

7 Post-analytical assessment of results, reflex testing[5] and reporting[2]

7.1 Key service requirements

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, or when more experienced staff should be consulted, depending on the results obtained and in line with national and local practice guidelines. Reporting of reference laboratory results should be as per local protocol
- the analyser and/or reagent kit used for each test should be recorded within the local quality management system. 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 laboratory accreditation
- reports generated must be concise, readable, standardised in format, and presented in a logical order. For example the test report should include the following items[3]: patient identifiers; the name and address of the laboratory location where the test was performed; the date and time of specimen collection; 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[2]

- significant results should be reviewed by the clinical infection team as soon as possible. Local SOPs should define which results require medical verification. The aim of review 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 to assist understanding of the end-user; and to recommend treatment/management or further follow-up investigations when clinically appropriate[2]
- urgent results should be communicated rapidly to appropriate bodies (including the requestor and public health professionals). Local SOPs and national regulations (see section 2: scientific information) should define which results require urgent communication, in order to facilitate timely clinical or public health interventions (including infection control precautions or provision of prophylaxis such as immunoglobulins)[2]
- results indicating certain communicable diseases should be electronically reported to Public Health England, or the equivalent public health body in devolved administrations (see section 2: scientific information). 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 (such as 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[2]
- routine biochemistry and haematology samples are stored in diagnostic laboratories for only a few days; however, a longer storage period is normally essential for microbial serology samples. The duration of storage should permit relevant additional testing, or the demonstration of seroconversion, in order to obtain a diagnosis[6]. The Infectious Diseases in Pregnancy Screening Programme Handbook for laboratories (October 2012) requires storage for a minimum of 2 years[7]. Safety of Blood, Tissues and Organs guidance[8] (SaBTO) advises storage of donor blood specimens for a minimum of 10 years and 30 years for recipient material[6]. 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[2]
- clinical results/reports, control data, and cleaning/maintenance records may be archived either on or off site, however, they must be easily and readily retrievable within an appropriate time frame if examination is needed

7.2 Medicolegal considerations

Refer to the joint Royal College of Pathologists / Institute of Biomedical Science document "Guidance for handling medicolegal samples and preserving the chain of evidence[9]".

8 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[2]
- local protocols should be put in place to manage the results of Quality Assessment (EQA) schemes[2], including investigation of failures

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

9 Evaluations, validations and verification of assays

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.

References

For the information on the reference assessment grades given, refer to the scientific information.

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9. The Royal College of Pathologists, Institute of Biomedical Science. Guidance for handling medicolegal samples and preserving the chain of evidence. 2017. **++**