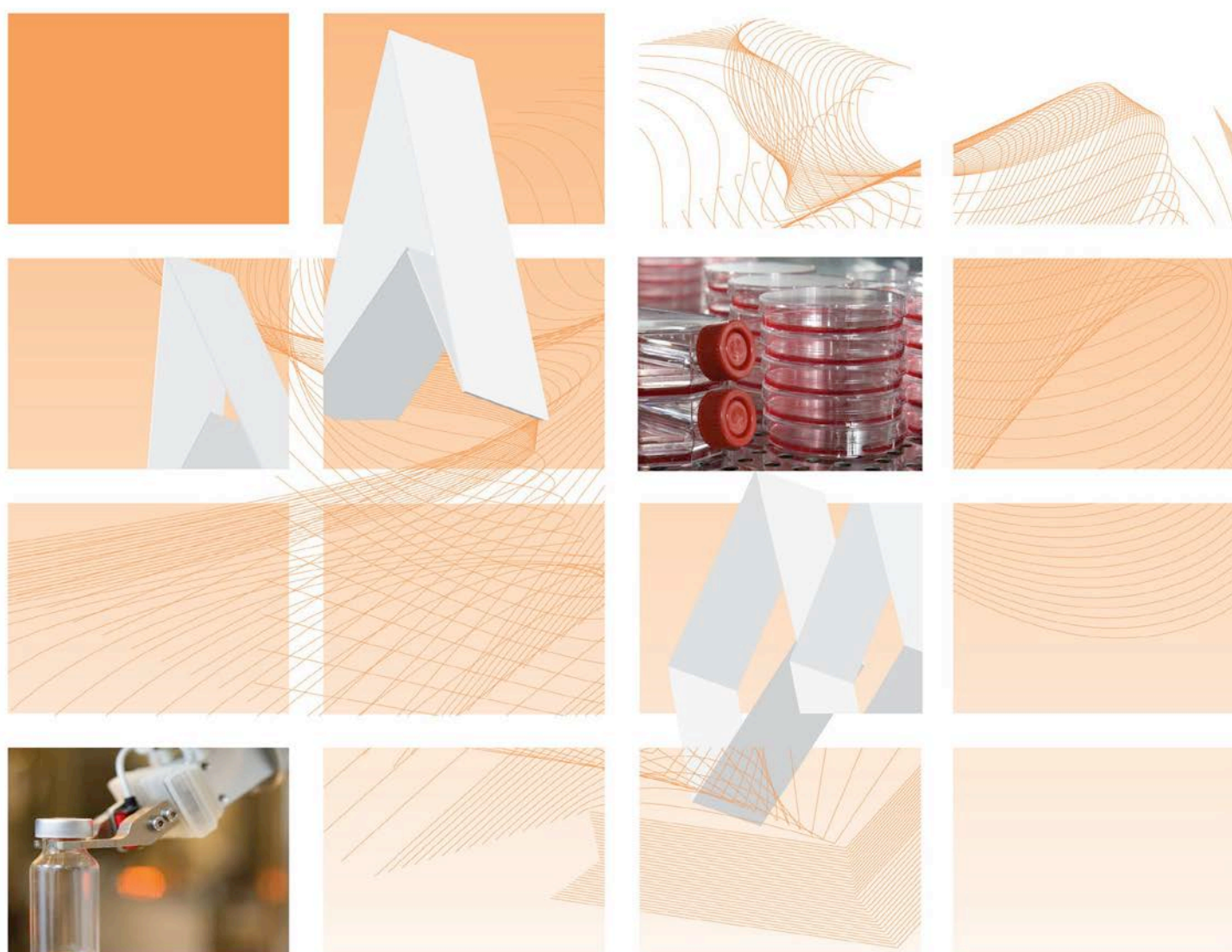




# UK Standards for Microbiology Investigations

## Good Laboratory Practice when Undertaking Serology Assays for Infectious Diseases



## Acknowledgments

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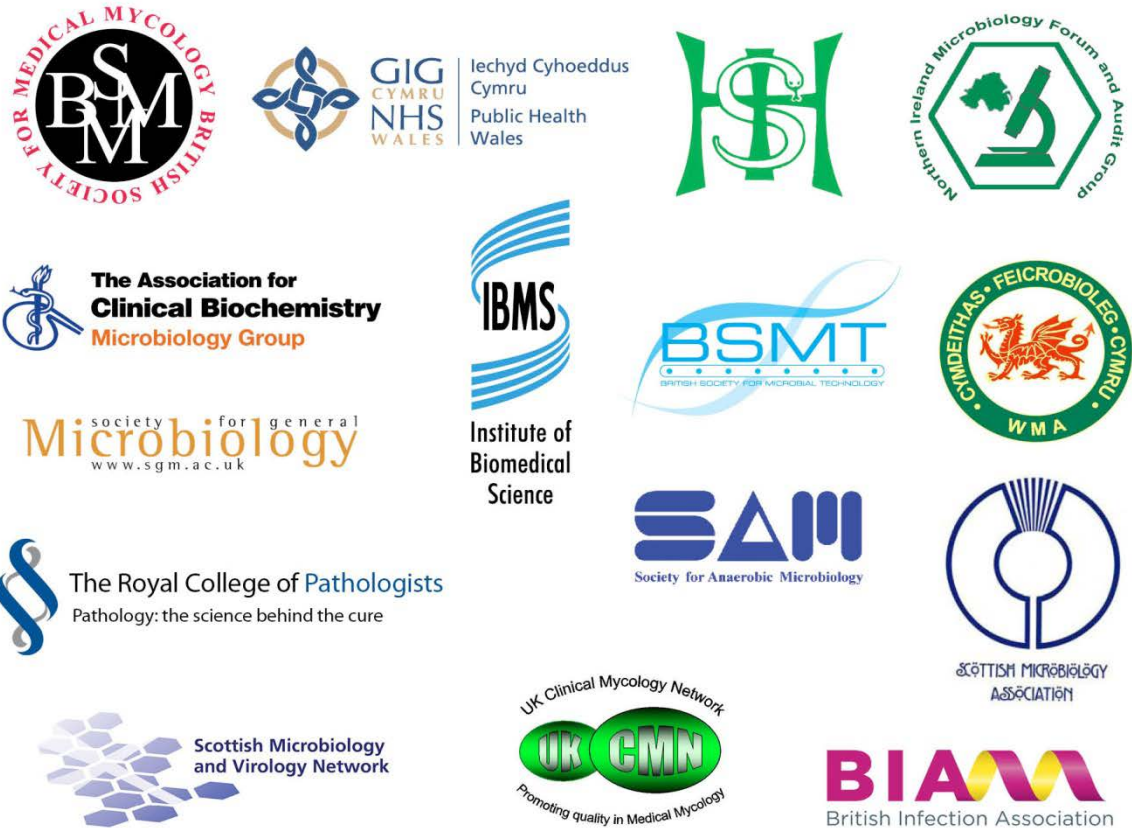
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NICE has accredited the process used by Public Health England to produce Standards for Microbiology Investigations. Accreditation is valid for 5 years from July 2011. More information on accreditation can be viewed at [www.nice.org.uk/accreditation](http://www.nice.org.uk/accreditation).

For full details on our accreditation visit: [www.nice.org.uk/accreditation](http://www.nice.org.uk/accreditation).

## Amendment Table

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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](mailto: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.	-/10.03.14
Issue no. discarded.	-
Insert Issue no.	1
<b>Section(s) involved</b>	<b>Amendment</b>

## UK Standards for Microbiology Investigations<sup>#</sup>: Scope and Purpose

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### 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.

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<sup>#</sup> 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](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.

### **Suggested Citation for this Document**

Public Health England. (2014). Good Laboratory Practice when Undertaking Serology Assays for Infectious Diseases. UK Standards for Microbiology Investigations. Q 7 Issue 1. <http://www.hpa.org.uk/SMI/pdf>.

## Scope of Document

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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 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 those 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.

This SMI should be used in conjunction with other SMIs.

## Introduction<sup>1-4</sup>

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

- There are many serology tests and NAATs, which can be requested 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. The availability of more than one test for each infection may also be confusing
- Many laboratories offer electronic Order Entry to an increasing proportion of their users. In this setting, listing all tests, or even a more limited selection, often leads to inappropriate requests. Conversely, when hand-written requests are received, it often requires considerable experience to determine what tests are requested or what tests may be appropriate in relation to the clinical details
- Serology testing can be fragmented across more than one pathology discipline (eg analysers in microbiology/virology and biochemistry)
- Serology results are not purely numerical results with “in-range” and “out-of-range” interpretations. The interpretation of microbial serology results is complex and is an essential component of a proper microbial serology service
- Many serology results must trigger appropriate, sometimes complex, reflex investigations which often involves testing on different analysers or sending to reference laboratories
- Further, or retrospective, testing is not uncommon and can be 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 Tests<sup>5</sup>

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Ordering on hand-written request cards is increasingly being replaced by electronic Order Entry systems. While requests on hand-written cards may not always be intelligible or give clear indications of what tests are required, Electronic Order Entry systems, offering extensive test menus, may lead to inappropriate or excessive requests.

Electronic Order Entry systems used for microbial serology tests should:

- include record of who placed the order, along with the contact details
- require the entry of relevant clinical details, as this often allows laboratory staff to reallocate the request to more appropriate tests
- require the entry of the date of onset of symptoms, when applicable, as for many serology tests a minimum interval is required for meaningful testing and interpretation
- require the entry of date(s) of exposure for testing following disease contact (eg pregnant woman exposed to a rash); Offer “syndromic order sets” in preference to individual tests whenever appropriate. This facilitates appropriate testing and reduces the risk of missed or delayed diagnosis. Situations in which testing for a panel of relevant infectious causes would normally be better practice than testing for individual virus include: acute hepatitis; glandular fever syndrome; lymphadenopathy; or culture-negative endocarditis<sup>6</sup>. Further examples of “syndromic order sets” are available via the [UK Standards for Microbiology Investigations](#) web pages
- 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 Tests<sup>7</sup>

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It is desirable that microbial serology requests adhere to a syndromic test selection, with minimum deviation. Test selection for individual 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 have more familiarity with infection terminology used in the clinical details; 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 local practices for pre-analytical assessment including:

- Indications for selecting “syndromic order sets”; staff may reallocate individual tests requests to “syndromic order sets” when appropriate

- Criteria for rejection: 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
- Criteria for re-allocation to different tests following discussion with requesting clinician: 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 reallocate the sample to hepatitis serology testing, if experienced scrutiny of the clinical details and any previous test results supports this course: Hepatitis B/C NAAT is usually appropriately requested only after a diagnosis of this infection is made based on serology tests
- Complex cases will require the involvement of the medical microbiologist or virologist in deciding what tests are appropriate. More information from the requesting practitioner, or a clinical review of the patient, may be required. The pre-analytical assessment 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 Specimens<sup>8</sup>**

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Analysis of the specimens should be conducted in conformity with 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 through analysers integrated into automated blood science tracks as well as free-standing analysers and manual assays. On some analysers “reflex testing” rules can be set up.

### **4 Post-Analytical Assessment of Results, Reflex Testing and Reporting**

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

- Additional “reflex” testing and confirmatory testing should be performed on the sample, if appropriate (the latter frequently via regional or national reference laboratories). The SOP of each serology test should specify what reflex or confirmatory tests may be required, depending on the results obtained and in line with national and local practice guidelines<sup>8</sup>
- 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
- Suitable interpretative comments should be appended to the results, when required, to make sure that the clinical user will 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<sup>9-11</sup>

- 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<sup>9-12</sup>
- 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)<sup>13</sup>
- 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 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 in advance of the electronic report by the medical microbiology staff, together with available information about the clinical presentation and interpretation<sup>13</sup>
- Whereas routine biochemistry and haematology samples are only stored in diagnostic pathology laboratories for a few days, 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 diagnosis<sup>14</sup>. The Infectious Diseases in Pregnancy Screening Programme Handbook for laboratories (October 2012) requires storage for a minimum of 2 years<sup>3</sup>. 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 stored specimens would be necessary in order to make a specific national recommendation on the length of storage<sup>15-17</sup>

## 5 Quality Assurance

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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](#).

Increasingly, microbial serology tests are being performed on machines integrated into blood sciences track systems. Under these circumstances, 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<sup>18</sup>
- 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<sup>12,19,20</sup>

It would be expected that 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 and Validations of assays<sup>21</sup>

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All assays used should have undergone suitable evaluations before being implemented for routine use in the laboratory in accordance with the principles laid out in [Q 1 – Commercial and In-House Diagnostic Tests: Evaluations and Validations](#).

## 7 Other Essential Components of a Good Microbial Serology Service

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- Regular audit of serology results, in particular those that assess the accuracy and positive 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 response to reactive screening results<sup>8,22</sup>
- There should be appropriate and relevant information in the laboratory users' guide/handbook. This will usually be an online document and should be regularly updated<sup>23,24</sup>
- Microbiologically trained 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 fashion<sup>12,19</sup>
- It is particularly important that there are expert microbiology personnel to formulate and implement rapid diagnostic responses to outbreaks and epidemiology alerts. New pathogens, like SARS or emerging influenza strains, occur with increasing frequency and often require the ability to set up and implement new testing or screening protocols at short notice<sup>12,19</sup>
- Microbiology staff will normally manage the appropriate use of specific immunoglobulins (eg VZIG, HBIG), either directly or via a collaborating pharmacy department<sup>12,19</sup>
- Microbiology staff should support and attend regular meetings with users of microbial serology and NAAT tests especially antenatal services, GUM and gastroenterology/hepatology<sup>25</sup>
- Microbiology staff should be involved in making supervisory arrangements for any point-of-care microbial serology tests<sup>1</sup>

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