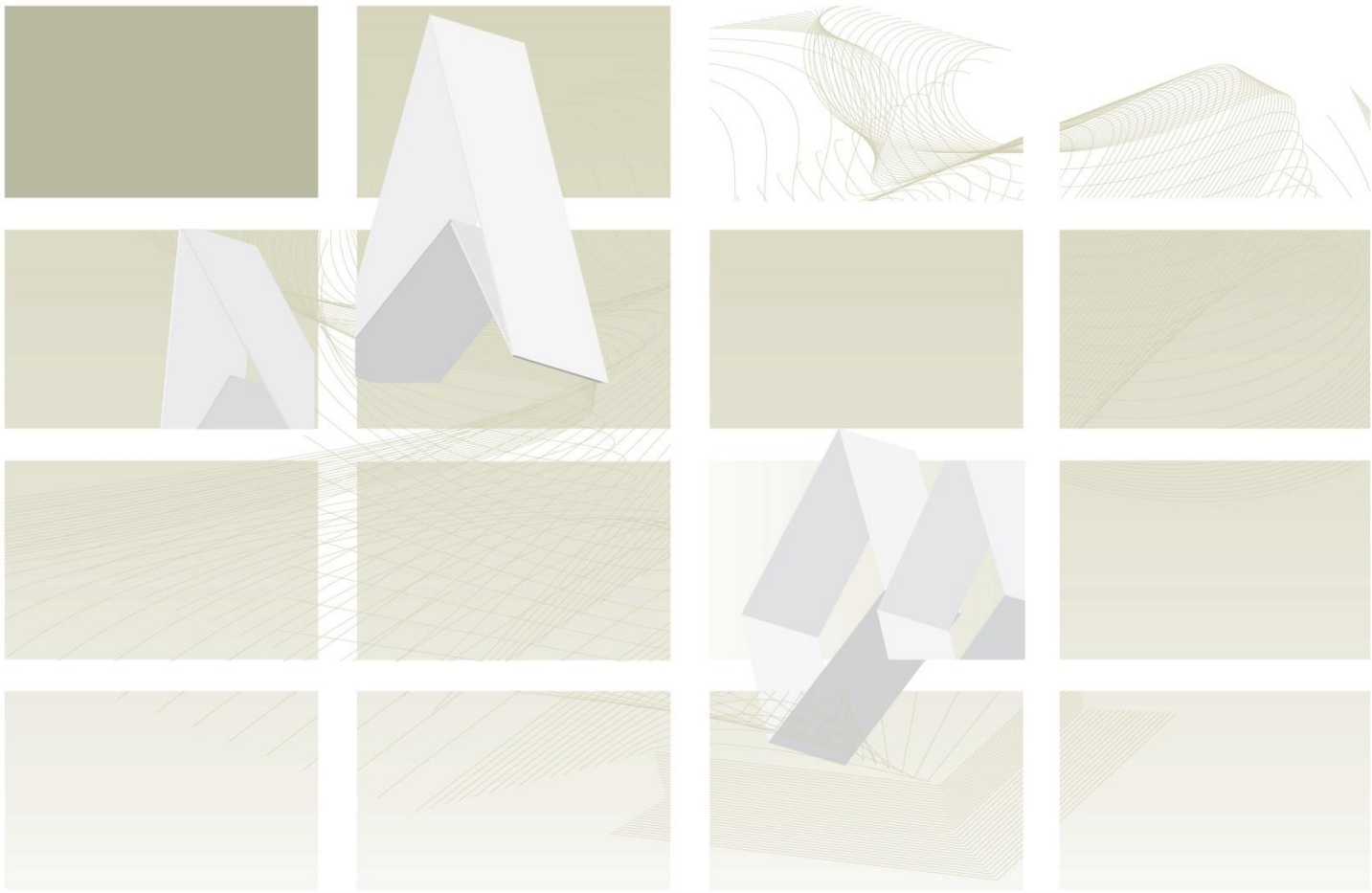
UK Standards for Microbiology Investigations

Review of users' comments received by
Working group for microbiology standards in clinical virology/serology

Q 7 Good practice when ordering and undertaking diagnostic tests for infectious disease serology



NICE accredited
www.nice.org.uk/accreditation

"NICE has renewed accreditation of the process used by **Public Health England (PHE)** to produce **UK Standards for Microbiology Investigations**. The renewed accreditation is valid until **30 June 2021** and applies to guidance produced using the processes described in **UK standards for microbiology investigations (UKSMIs) Development process, S9365', 2016**. The original accreditation term began in **July 2011."**

This publication was created by Public Health England (PHE) in partnership with the NHS.
Recommendations are listed as ACCEPT/ PARTIAL ACCEPT/DEFER/ NONE or PENDING

Consultation: 27/01/2021 – 10/02/2021

Version of document consulted on: Q 7 de+

Section for comments 3 – Scope of document

Comment number: 1

Date received: 04/02/2021
Laboratory/organisation name: Severn Infection Sciences and Bristol PHL

- General- I suggest that somewhere in this document there is an expression of recognition that electronic order communication systems have been designed to eliminate some of the control and checking elements that are recommended in the text. Realism should be reflected around the ability to triage requests by any grade of staff. Better to focus on the front end design of order comms and mention back-up advice to be found in the user manual. Also see uploaded file.

Recommended action

1. PARTIAL ACCEPT: A sentence has been added to section 5 referring to local user manuals

Section for comments 4 - Introduction

Comment number: 2

Date received: 04/02/2021
Laboratory/organisation name: Severn Infection Sciences and Bristol PHL

- First bullet point- I agree there are many tests, but actually the test types are mostly restricted to IgG and IgM EIA. again, the large choice of tests confuses the user when the advisory statements are not available on order comms or in user manual.
- Second bullet point- wrong emphasis. Order comms should make it easier, not bewildering (a word I suggest removing). How about 'A poorly designed electronic order system can lead to....'
- Bullet 5- which staff are you referring to regarding interpreting results? If microbiology then that should be part of standard training, if clinical non-laboratory, how do you suggest this is achieved?

Recommended action

1. ACCEPT: a note covering use of advisory statements has been added
2. ACCEPT: bullet point has been rephrased
3. PARTIAL ACCEPT: bullet point has been rephrased

Comment number: 3

Date received:
Laboratory/organisation name: Institute of Biomedical Science

- Page 6 first bullet point (third in section 4)

Fragmentation may not only occur over more than one pathology discipline. Fragmentation may now occur over laboratories in a network over large geographic areas.

- Page 6 final bullet point in section 4
  Outside of SABTO and ANC guidelines, it is the RCPath guidelines for retention and storage that are generally followed. Will the RCPath be asked to review and update its retention and storage guidelines in line with the need for longer storage of serology samples?

Recommended action

1. ACCEPT: the bullet point has been updated to reflect that fragmentation may occur over multiple sites
2. NONE: the RCPath guidelines are referenced in the bullet point; if further guidance is released the UK SMIs will be updated in line with this

Comment number: 4

Date received: 10/02/2021
Laboratory/organisation name: Diagnostic Development and Evaluations Unit (DDEU)

It would be helpful to have a fuller explanation of serology, either as a paragraph or to provide a suitable reference or link (either in the scope or introduction sections). This could include the circumstances when different antibody tests (IgG/IgM/IgA etc) or antigen tests are applied; and to give an overview of the different serology technologies (e.g. EIAs, automated platforms, Lateral Flow Devices, LFDs. Confirm if the document relates to laboratory-based serology assays only. LFDs can be for lab professional use, clinics, or for home self-testing etc

Recommended action

1. NONE: UK SMIs should be used in conjunction with other relevant UK SMIs, which will cover different testing technologies where applicable.

Section for comments 5 – Ordering microbial serology tests

Comment number: 5

Date received: 08/02/2021
Laboratory/organisation name: NHS Lothian

- Please can we add a section about checking the local guidance on specimen collection tubes and instructions for handling the samples. Some tests require to be collected at specific times and require special blood tubes e.g whole blood samples for microfilariae. These may require alerting the laboratory to ensure they are processed correctly.
- Please can we also add something about ensuring that there is an adequate amount of blood for the number of tests required. There is a limit to how many tests you can do on 2mls of serum.

Recommended action

1. ACCEPT: a sentence has been added advising that local user manuals should be consulted

2. NONE: detail on specimen collection is out of scope for this document, and is instead covered by individual UK SMIs. This will also be covered by local user manuals

Comment number: 6

Date received: 09/02/2021
Laboratory/organisation name: Abbott

Where the document states 'there are many serology tests and NAATs available to diagnose bacterial, viral, fungal or parasitic infections.', we would suggest amending to read 'to support diagnosis of or evidence of infection by'. Serology tests are rarely used to diagnose viral infections, for example.

Recommended action

1. ACCEPT: wording has been amended

Comment number: 7

Date received: 10/02/2021
Laboratory/organisation name: Diagnostic Development and Evaluations Unit (DDEU)

P 5 (last sentence is incomplete) Conversely, when hand-written requests are made.

Recommended action

1. NONE: the sentence wraps on to the following page

Section for comments 6 – Pre-analytical assessment of microbial serology tests

Comment number: 8

Date received: 04/02/2021
Laboratory/organisation name: Severn Infection Sciences and Bristol PHL

Unrealistic to expect laboratory based staff to oversee test selection in any way other than in a governance perspective- I cannot see how every test can be reviewed at receipt. Intermittent audit is a more achievable way of checking requests are suitable. Adding tests not directly requested: I suggest expressing caution here over consent issues. it is acceptable to add tests when a broad request is made such as 'viral hepatitis please' or to validate initial results, but if specific requests are made consent cannot be implied for others- for example, lymphadenopathy requesting EBV but not HIV- I doubt HIV can be added without asking.

Recommended action

1. NONE: oversight of test selection is not suggested for every test, rather “when required”, “in line with local procedure”. Reference to clinical coding protocol has been added
2. ACCEPT: a sentence on consideration of consent requirements has been added to the bullet point on adding additional tests

Comment number: 9

Date received:
Laboratory/organisation name: Institute of Biomedical Science

- Page 7 fourth bullet point
  This could be confusing and would be clearer it if was written as "reallocating to a serological test ..." (i.e. remove the 'non')

Recommended action

1. ACCEPT: sentence has been reworded

Comment number: 10

Date received: 09/02/2021
Laboratory/organisation name: Abbott

Where the document states 'A hepatitis B and hepatitis C NAAT request is usually appropriate only after a diagnosis of this infection is made based on serology tests', we would suggest that the guidance additionally states 'Where there is a suspicion of a recent infection NAAT or antigen testing may confirm infection prior to seroconversion. A repeat sample may be also required where an acute viral infection is a possibility, such as post-needle stick injury.'

Recommended action

1. PARTIAL ACCEPT: A note has been added directing users to the relevant UK SMIs covering hepatitis B and hepatitis C

Comment number: 11

Date received: 10/02/2021
Laboratory/organisation name: Diagnostic Development and Evaluations Unit (DDEU)

Consider reducing the number of times NAATs is mentioned in the document e.g. to devote one paragraph to the similar points made about this across the document.

Recommended action

1. NONE: NAATs are mentioned where relevant in each section

Section for comments 7 – Post-analytical assessment of results, reflex testing and reporting

Comment number: 12

Date received: 27/01/2021
Laboratory/organisation name: Guy's & St Thomas' NHS Foundation Trust

While the post-analytical section mentions decisions to forward samples to reference laboratories, the resulting section makes no mention of the handling of the result from such laboratories. Could we suggest that reference laboratory results returned to the local clinical laboratory are added to the patient medical record (electronic or paper) and/or that the requesting clinician will have a way of accessing such results.

Recommended action

1. PARTIAL ACCEPT: A sentence has been added stating that reference laboratory results should be reported as per local protocol

Comment number: 13

Date received: 04/02/2021
Laboratory/organisation name: Severn Infection Sciences and Bristol PHL

- Bullet 2- clarify if the advice is to record the manufacturer and kit on the report, or just within laboratory systems.
- Bullet 5- suggest change 'verified' to 'reviewed'. Consider whether this SMI is asking clinicians to check the technical output of a significant result- this is not realistic. In addition, there is a logical argument that the less significant results should have similar technical checks.

Recommended action

1. ACCEPT: “within the local quality management system” has been added to clarify this point
2. ACCEPT: bullet point has been amended

Comment number: 14

Date received: 09/02/2021
Laboratory/organisation name: Society for Applied Microbiology

As this document specifically concerns diagnostic tests based on serology (although it also mentions nucleic acid amplification tests), it should advocate the use of international standards to calibrate and harmonise assay data (probably in section 7.1) as far as possible and the standards exist.

Recommended action

1. NONE: this is within the scope of UK SMI Q 2, and therefore not covered in Q 7

Comment number: 15

Date received: 09/02/2021
Laboratory/organisation name: Society for Applied Microbiology

Bullet 2 "The analyser and/or reagent kit used for each test should be recorded." We suggest elaborating on this by inserting a comment that cites the UK SMI that builds upon this and has ISO 15189-style best practice info about e.g. supplier choice, testing procedures determination.

Recommended action

1. NONE: this is covered within the scope of UK SMI Q 1, and therefore not covered in Q 7

Comment number: 16

Date received: 09/02/2021
Laboratory/organisation name: Society for Applied Microbiology

- Bullet 5 - 'Significant results (for instance those suggesting a recent infection), should be verified by medical microbiology staff.'
    i. We question why only 'recent' should be verified and suggest rewording to "current."
    ii. We suggest adding a specified time interval in case of e.g. unsuspected sepsis – as medical verification may be speedily needed. As the next bullet point only partly covers this second point, we suggest further clarification.

Recommended action

1. ACCEPT: bullet has been reworded to state that “significant results should be reviewed by clinical infection team as soon as possible”
2. NONE: specific time intervals are outside the scope of this UK SMI

Comment number: 17

Date received:
Laboratory/organisation name: Institute of Biomedical Science

- 7.1 Key service requirements second bullet point
  The analyser and kit reagent details should always be recorded in the laboratory anyway. It is not necessary to include this information on the patient results report (it is not clear whether this is what is being suggested, so perhaps the wording of that point or the ordering of the bullet points could be reviewed).

Recommended action

1. PARTIAL ACCEPT: bullet point has been amended to specify that analyser/and or reagent kit used for each test should be recorded within the local quality management system

Comment number: 18

Date received: 09/02/2021
Laboratory/organisation name: Abbott

- Where the document states '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 guidelines' we would like to propose that the guidance could require each laboratory, including regional and national reference laboratories, to publish their algorithms so service users are aware of all steps and requirements and why. This should also helps health care scientists to achieve national harmonisation. By publishing their guidelines officially, they will always need to renew them and readdress suitability within their quality system. This transparency would also help biomedical scientists sending off referrals to reference labs, leading to fewer mistakes and improved outcomes for the patient.

Recommended action

1. NONE: laboratory algorithms are covered in individual UK SMIs, which laboratories may adopt

Comment number: 19

Date received: 09/02/2021
Laboratory/organisation name: Abbott

- Where the document states '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', we would like to propose that this guidance could support Microbiology Labs towards adopting multi-disciplinary harmonisation of result interpretation. Most, if not all, UK labs have LIMS systems able to manage multidisciplinary data. Multidisciplinary harmonisation approach can enhance microbiological investigations, for example recent infection can be immediately supported by inflammatory markers/coagulation test results from blood sciences. Also in the investigation of hepatitis. microbiology results in conjunction with biochemical tests can differentiate between liver dysfunction caused by virus versus lifestyle. So guidance to identify the complete testing protocol best suited for the service user could improve diagnosis and outcomes of infectious disease, reduce multiple sample requirements and the risk of missing or available samples.

Recommended action

1. NONE: the use of multidisciplinary data is common practice within infection sciences

Comment number: 20

Date received: 09/02/2021
Laboratory/organisation name: Abbott

- We have additional comments to support the statements in the paragraph that describes microbiology sample storage. There is a lack of standardisation in storage of microbiology blood samples, as acknowledged in this guidance. We can add some observations for consideration;
    - Capacity for storage varies between laboratories, and this is impacted by sample container types, for example many UK labs use 75 x 13mm aliquot tubes which take up huge amounts of freezer space whereas others use 96 well microtiter plates that are small and compact.
    - Sample volume for storage varies greatly with some labs trying to take the maximum amount of sample for long term storage whereas others (those that store in microtiter plates) will take a fixed volume for storage.
    - Storage temperature varies across UK labs with some labs storing samples at -20°C and others at -80°C; there is a significant difference in the cost and capacity requirements.

  So a recommendation for consideration would be to create national guidance for microbiology laboratories to store a minimum volume sample required for additional tests, in the smallest physical aliquot (microtiter plate) in the most appropriate freezer. This could lead to increased availability of lab space, fewer freezers, lower power requirements and less plastics used. Microbiology labs should ensure that their sample storage requirements/obligations are communicated to and prioritised by other blood testing departments; there are examples where a single blood tube is received and sent away for mass

spectrometry/referral testing such as vitamin D and all the serum is utilised before microbiology has been able to store it.

Recommended action

1. NONE: This level of detail is out of scope for UK SMI Q 7; users may refer to RCPath guidelines for further detail on storage and retention of samples

Comment number: 21

Date received: 10/02/2021
Laboratory/organisation name: Diagnostic Development and Evaluations Unit (DDEU)

It may be helpful to expand on what is meant by reflex testing. Not all readers will be familiar with this term. Where it states that 'urgent results should be communicated rapidly to appropriate bodies' it would be helpful to indicate what should happen in practice e.g. if this means an initial phone call to provide a verbal result, and/or a preliminary LIMS generated report.

Recommended action

1. NONE: definitions of reflex (and reflective) testing are given in the reference “Srivastava R, Bartlett WA, Kennedy IM, Hiney A, Fletcher C, Murphy MJ. Reflex and reflective testing: efficiency and effectiveness of adding on laboratory tests. Annals of Clinical Biochemistry 2010;47:223-7” cited in this document
2. NONE: laboratories will specify the mechanism for (and format of) communication of urgent results in local SOPs

Section for comments 8 - Quality assurance

Comment number: 22

Date received:
Laboratory/organisation name: Institute of Biomedical Science

- Page 9 final bullet
  In situations, such as hub/spoke laboratories, where microbiology tests are done on a blood science analyser and there are no trained microbiology staff on site, provision should be made for monitoring and EQA of samples and QA failure investigations to be undertaken remotely by appropriately qualified microbiology staff.

Recommended action

1. PARTIAL ACCEPT: sentence has been rephrased to state that local protocols should be put in place to mange QA activities and investigation of failures

Comment number: 23

Date received: 10/02/2021
Laboratory/organisation name: Diagnostic Development and Evaluations Unit (DDEU)

- Section 8: Provide guidance on quality assurance for Lateral Flow Devices
- Section 9:

a) Consider mentioning in relation to GB that SARS-CoV-2 serology devices should be validated according to MHRA's Target Product Profile (TPP) for serology assays.
b) For commercial IVDS note that CE IVDs (or devices with equivalent quality mark e.g. UKCA) should be deployed

Recommended action

1. NONE: LFDs are not covered in the scope of UK SMI Q 7
2. NONE: CE marking is covered in the scope of UK SMI Q 1, and therefore is not covered in the scope of UK SMI Q 7

Section for comments References

Comment number: 24

Date received: 08/02/2021
Laboratory/organisation name: NHS Lothian

I have read the document three times and I cannot find where reference 6 is cited. Is it redundant? Gould FK, Denning DW, Elliott TS, Foweraker J, Perry JD, Prendergast BD et al. Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party ofthe British Society for Antimicrobial Chemotherapy. J AntimicrobChemother 2012;67:269-89.

Recommended action

1. NONE: the reference is cited in section 5 “ordering microbial tests” under bullet point 3

Section for comments General comment

Comment number: 25

Date received: 04/02/2021
Laboratory/organisation name: Severn Infection Sciences and Bristol PHL

Title - 'Undertaking' diagnostic tests normally means the act of performing the test- I don't think that applies to this SMI.

Recommended action

1. NONE: Following discussion by the Virology Working Group, no further amendment to the title has been made

Comment number: 26

Date received: 04/02/2021
Laboratory/organisation name: Clinical Microbiology, Truro, Cornwall

- Avoidance of cross-contamination – low level cross contamination of samples is of little consequence for most biochemical analytes since it can only cause a very small percentage change in the final result. Conversely, accidental transfer of very small volumes of serum between a positive and negative sample can result in falsely positive results in very sensitive virology assays such as those used to

detect hepatitis B or HIV infection. The consequences of such results is clinically very significant and has previously caused SUIs. If cross-contamination affects samples held in storage it can be impossible to determine the true result without procuring further specimens from the patient. To avoid these issues, only analysers with robust mechanisms to prevent cross-contamination should be used for infectious disease serology. This should be assessed locally and form part of the verification of new equipment and re-evaluated at intervals. Aliquots of sera stored for future testing should be separated in a way that prevents contamination before the sample enters the testing platform, especially where testing takes place on the primary specimen.

Recommended action

1. NONE: evaluation and verification of equipment is covered in the scope of UK SMI Q 1, and therefore is not included in the scope of Q 7

Comment number: 27

Date received: 04/02/2021
Laboratory/organisation name: Clinical Microbiology, Truro, Cornwall

- Choice of assays - Multi-discipline analysers necessarily have a limited range of virological assays available. In many cases these are closed systems and only one assay produced by the analyser's manufacturer is available for each analyte. In this situation, laboratories should ensure that clinical need and analytical performance drive the choice of tests performed by the laboratory. Where the assays produced by the analyser manufacturer are either not available or inadequate, it will be necessary to use other assays or platforms which may incur extra cost or inconvenience.

Recommended action

1. NONE: evaluation of equipment is covered in the scope of UK SMI Q 1, and therefore is not included in the scope of Q 7

Comment number: 28

Date received: 09/02/2021
Laboratory/organisation name: Society for Applied Microbiology

- To be used legally, in vitro diagnostic (IVD) tests should comply with the relevant parts of the Medical Devices Regulations (200) and be CE marked or otherwise derogated officially by the MHRA. We believe SMI Q1 still mentions the EU IVD Directive. This will have been translated in UK law post-Brexit but perhaps the SMI documents need to be revised to reflect this.

Recommended action

1. NONE: CE marking is covered in the scope of UK SMI Q 1, and therefore is not covered in the scope of UK SMI Q 7

Comment number: 29

Date received: 09/02/2021
Laboratory/organisation name: Society for Applied Microbiology

- Title - While UK SMIs often use the word 'Good', we suggest changing it from 'Good' to 'Best' as ''Good'' is a bit too close to ''Good Lab Practice'' with its QA implications.

Recommended action

1. NONE: Following discussion by the Virology Working Group, no further amendment to the title has been made

Comment number: 30

Date received:
Laboratory/organisation name: Institute of Biomedical Science

- It should be made transparently clear throughout the document that the specimen requirements for NAAT test and serology may be different. So it may not always be possible to reallocate the sample from one a request for one type of test to the other. NAATs usually require whole blood (EDTA) samples and a maximum time of transport to the laboratory . Although the document is mostly considering changing from NAATs request to serology instead, this should be clearly explained. As guidance, it should be clear that the specimens would not necessarily be interchangeable. So a clinician requesting a NAATs test appropriately should be aware of the requirement. Perhaps a note saying specimen requirements for NAATs should be discussed with the receiving laboratory.

Recommended action

1. ACCEPT: a note has been added to section 5 to cover this point

Comment number: 31

Date received: 09/02/2021
Laboratory/organisation name: Abbott

- The 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'. We suggest that the previous title may be more accurate as serology tests are not limited to diagnostic use, looks for signs of an active, current infection. Many serology tests are not approved for making a diagnosis, and many and limited for use in aiding a diagnosis. Serology tests may be performed for non diagnostic applications such as screening for antenatal/organ or blood donations, confirmation testing, patient follow up or to confirm antibody levels post vaccination (eg HepB).

Recommended action

1. NONE: following discussion at the Virology Working Group, no further amendment to the title has been made

Comment number: 32

Date received: 10/02/2021
Laboratory/organisation name: Diagnostic Development and Evaluations Unit (DDEU)

The word 'ordering' could be easily confused with ordering kits/supplies from the manufacturer. Would it be better to replace this with 'requesting (tests)', so that the title would read 'Good practice when requesting and undertaking diagnostic tests for infectious disease serology'. This also applies to other mentions of 'ordering' through the document.

Recommended action

1. NONE: following discussion at the Virology Working Group, no further amendment to the title has been made

Section for comments Financial barriers

Respondents were asked “are there any potential organisational and financial barriers in applying the recommendations or conflict of interest?”.

Comment number: 33

Date received: 27/01/2021
Laboratory/organisation name: Guy's & St Thomas' NHS Foundation Trust

No

Comment number: 34

Date received: 04/02/2021
Laboratory/organisation name: Severn Infection Sciences and Bristol PHL

Consider realism in applying the advice about triaging and checking requests

Comment number: 35

Date received: 04/02/2021
Laboratory/organisation name: Clinical Microbiology, Truro, Cornwall

No conflict of interest. Implementing them should inform the procurement process. It could cause organisational upset if it means that samples can't be processed on bulk analysers for some tests.

Comment number: 36

Date received: 08/02/2021
Laboratory/organisation name: NHS Lothian

No

Comment number: 37

Date received: 09/02/2021
Laboratory/organisation name: Society for Applied Microbiology

No

Comment number: 38

Date received:
Laboratory/organisation name: Institute of Biomedical Science

No response given

Comment number: 39

Date received: 09/02/2021
Laboratory/organisation name: Abbott

None anticipated

Comment number: 40

Date received: 10/02/2021
Laboratory/organisation name: Diagnostic Development and Evaluations Unit (DDEU)

No

Section for comments Health benefits

Respondents were asked “are you aware of any health benefits, side effects and risks that might affect the development of this UK SMI?”.

Comment number: 41

Date received: 27/01/2021
Laboratory/organisation name: Guy's & St Thomas' NHS Foundation Trust

No

Comment number: 42

Date received: 04/02/2021
Laboratory/organisation name: Severn Infection Sciences and Bristol PHL

No response given

Comment number: 43

Date received: 04/02/2021
Laboratory/organisation name: Clinical Microbiology, Truro, Cornwall

No response given

Comment number: 44

Date received: 08/02/2021
Laboratory/organisation name: NHS Lothian

No

Comment number: 45

Date received: 09/02/2021
Laboratory/organisation name: Society for Applied Microbiology

No response given

Comment number: 46

Date received:
Laboratory/organisation name: Institute of Biomedical Science

No response given

Comment number: 47

Date received: 09/02/2021
Laboratory/organisation name: Abbott

None anticipated

Comment number: 48

Date received: 10/02/2021
Laboratory/organisation name: Diagnostic Development and Evaluations Unit (DDEU)

No

Section for comments Interested parties

Respondents were asked “are you aware of any interested parties we should consider consulting with on the development of this document

Comment number: 49

Date received: 27/01/2021
Laboratory/organisation name: Guy's & St Thomas' NHS Foundation Trust

No response given

Comment number: 50

Date received: 04/02/2021
Laboratory/organisation name: Severn Infection Sciences and Bristol PHL

No response given

Comment number: 51

Date received: 04/02/2021
Laboratory/organisation name: Clinical Microbiology, Truro, Cornwall

No response given

Comment number: 52

Date received: 08/02/2021
Laboratory/organisation name: NHS Lothian

No

Comment number: 53

Date received: 09/02/2021
Laboratory/organisation name: Society for Applied Microbiology

No response given

Comment number: 54

Date received:
Laboratory/organisation name: Institute of Biomedical Science

No response given

Comment number: 55

Date received: 09/02/2021
Laboratory/organisation name: Abbott

No response given

Comment number: 56

Date received: 10/02/2021
Laboratory/organisation name: Diagnostic Development and Evaluations Unit (DDEU)

No