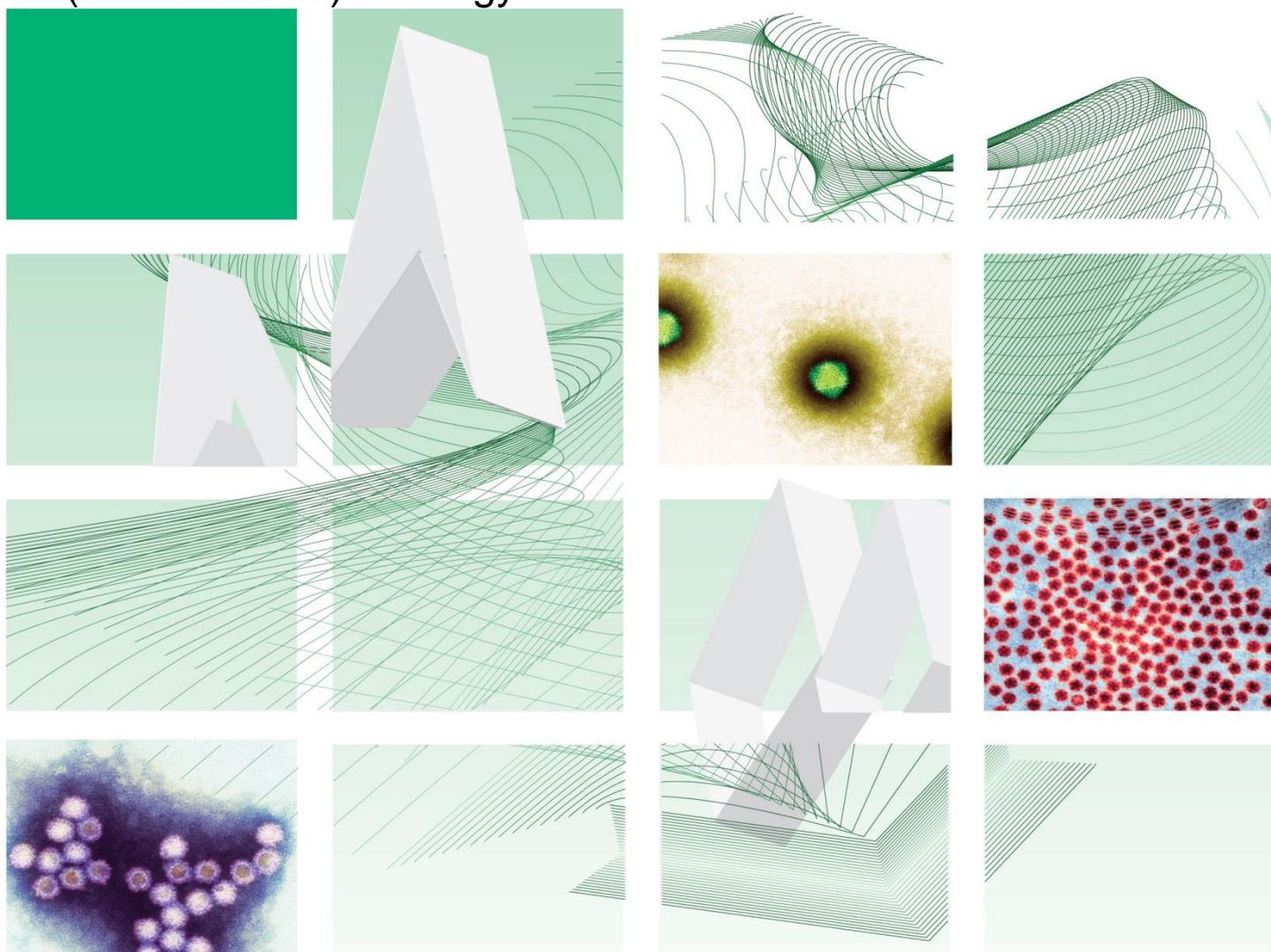


UK Standards for Microbiology Investigations

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) serology



"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.

Issued by the Standards Unit, National Infection Service, PHE

Virology | V 58 | Issue no: 1 | Issue date: 05.10.2020 | Page: 1 of 11

PHE publications gateway number: GW-1365

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Acknowledgments

UK Standards for Microbiology Investigations (UK SMIs) are developed under the auspices of 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>. UK 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.

PHE publications gateway number: GW-1365

UK Standards for Microbiology Investigations are produced in association with:



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Amendment table

Each UK 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 number/date	-/05.10.2020
Issue number discarded	-
Insert issue number	1
Anticipated next review date*	05.10.2023
Section(s) involved	Amendment
-	-

*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

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus SARS-CoV-2¹. Most people infected with SARS-CoV-2 will experience mild to moderate respiratory illness and recover without requiring special treatment¹. Black, Asian and Minority Ethnic (BAME) patients, older people, and those with underlying medical problems such as cardiovascular disease, diabetes, chronic respiratory disease and cancer are more likely to develop serious illness².

Seroprevalence testing programmes are being rolled out across all 4 nations of the UK with different approaches for testing certain key workers and/or patients. These antibody testing programmes aim to provide information on the prevalence of COVID-19 in different regions of the country and help better understand how the disease spreads. The programmes will work alongside PCR testing which confirms whether someone currently has the virus.

This UK SMI describes a testing algorithm which supports the antibody testing programme and gives indications to the laboratories on how to interpret results from approved commercial serological kits.

Refer to [Q1 - Evaluations, validations and verifications of diagnostic tests](#) and [Q 7 - Good practice when undertaking serology assays for infectious diseases](#) for information regarding good laboratory practice in serological testing.

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

4. Background

Serological assays for SARS-CoV-2 detect the antibody-based immune response to infection caused by the virus. Unlike methods which detect the genetic material (and thus the presence) of the virus, antibody tests could potentially help to determine that an individual has been exposed to the virus immunologically, whether they have displayed COVID-19 symptoms or not.

Correlates of immunity to SARS-CoV-2 infection are not yet well defined. Therefore, at present, positive serological assays cannot be used to infer protective immunity against SARS-CoV-2 or as a sole-method for the diagnosis of COVID-19 disease.

Thus, the role of serology is currently limited to indicating whether someone has had the virus or not, and to guiding epidemiological and public health control measures by providing information of the level and length of the immune response following SARS-CoV-2 viral infection. This information will be useful to determine how the virus spreads across the country, especially in health and social care workers and those at higher risk of clinical complications.

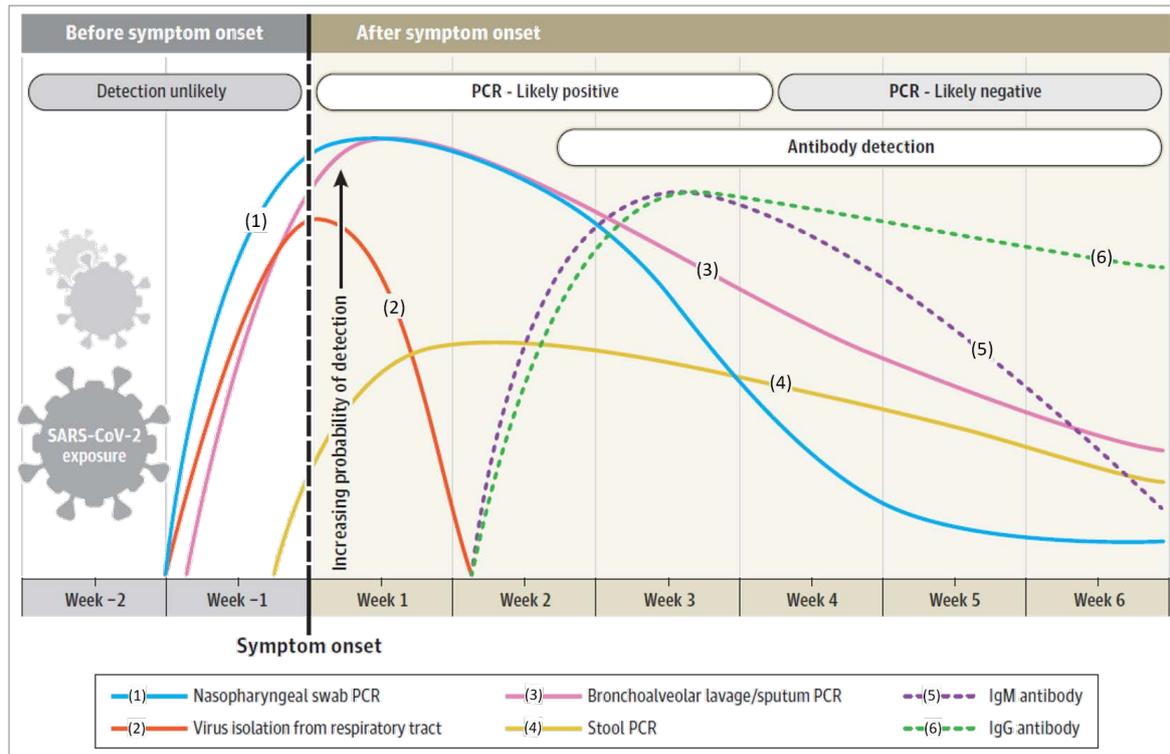


Figure 1: Estimated variation over time in diagnostic tests for detection of SARS-CoV-2 infection relative to symptom onset ³

In symptomatic, immunocompetent individuals, SARS-CoV-2 will normally elicit the development of IgM and IgG antibodies. Early in SARS-CoV-2 infection (first 7 days) the adaptive immune response begins to develop, and antibodies may not yet be detectable. IgG and IgM antibodies are increasingly likely to be detected from 7 days after the onset of symptoms. The majority of individuals will have a detectable antibody response ⁴. IgM levels then begin to decline, reaching lower levels by week 5 and almost disappearing by week 7, while IgG levels persist beyond 7 weeks³.

Asymptomatic and/or immunocompromised individuals may show a delayed or absent antibody response to SARS-CoV-2 infection⁵. As more data become available, understanding of the antibody response will increase.

Antibody testing in the UK

Coronaviruses have four structural proteins: the spike protein, nucleocapsid, envelope protein and membrane protein. Existing assays target antibodies to the nucleocapsid and/or spike proteins. The nucleocapsid protein is highly immunogenic and induces an earlier antibody response than the spike protein during infection, making it an attractive protein for diagnostic assay design. The spike protein is also relatively immunodominant, consisting of two subunits: the S1 protein containing the receptor binding domain (RBD); and the S2 protein which mediates fusion of the virus particle to the cell membrane⁶. Sequence homology of the nucleocapsid and spike proteins of SARS-CoV-1 to other *Betacoronaviruses* is 33 to 47% and 29% respectively⁷. SARS-CoV-2 is similar to SARS-CoV-1, showing sequence homology of 90% in the nucleocapsid and 76% in the spike protein⁸.

Commercially-available serological assays can detect IgG alone, or both IgG and IgM (total antibody)⁹. Evaluation of commercial kits by PHE, using serum samples from PCR-positive individuals, has shown no substantive differences in sensitivity of assays whether they test for IgG or total antibodies

(<https://www.gov.uk/government/publications/covid-19-laboratory-evaluations-of-serological-assays>).

Antibodies detected in an assay which includes spike proteins as an antigen may have a closer correlation with the presence of neutralising antibodies against SARS-CoV-2¹⁰.

5. Safety considerations

This guidance should be supplemented with local COSHH and risk assessments. Refer to current guidance on the safe handling of all organisms documented in this UK SMI.

For safe handling and processing for COVID-19 related samples in laboratories please refer to PHE guidance:

<https://www.gov.uk/government/publications/wuhan-novel-coronavirus-guidance-for-clinical-diagnostic-laboratories/wuhan-novel-coronavirus-handling-and-processing-of-laboratory-specimens>

6. Specimen processing and procedure

6.1 Specimen type

Blood, serum or plasma (follow manufacturers' specifications)

6.2 Specimen transport and storage conditions

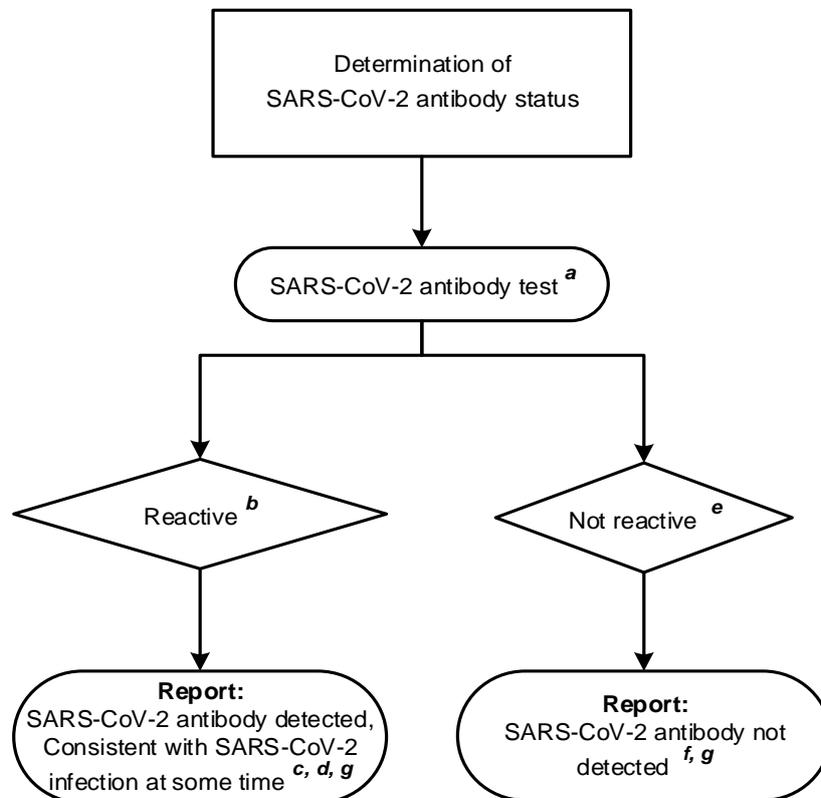
Specimens should be collected in appropriate CE marked leak proof containers and transported in sealed plastic bags according to UK regulations.

Specimens should be transported and processed according to manufacturers' instructions or local validation data¹¹.

Samples should be retained in accordance with The Royal College of Pathologists guidelines 'The retention and storage of pathological records and specimens'¹²

7. Investigation

Detection of SARS-CoV-2 antibodies



Please note: Interpretation and use of equivocal results will depend on manufacturer instructions and on local validation data.

Footnotes relating to detection of SARS-CoV-2 antibodies algorithm:

- a) Antibody test refers to IgG or total antibody assay.
- b) Consideration should be given to the possibility of a false positive result. The likelihood of false reactivity depends on local seroprevalence.
- c) Data not currently available to support the use of a reactive result to exclude the possibility of re-infection.
- d) Data not currently available on how IgG correlates to functional immunity, therefore a reactive result cannot be interpreted to mean that the patient is immune, or that they are not currently infected, and/or that they cannot transmit the virus to others.
- e) Immunocompromised individuals may not mount a detectable antibody response or may present a delayed response.
- f) This result does not exclude recently acquired infection (7 to 14 days after symptom onset). Please send an appropriate respiratory sample for SARS-CoV-2 PCR if symptomatic.
- g) Every report should include the assay manufacturer, the antibody class(es) and the target antigen(s).

8. Interpreting and reporting laboratory results

Interpretation and reporting table for Detection of SARS-CoV-2 antibodies:

	SARS-CoV-2 antibodies	Interpretative Comment	Notes
1	Reactive	SARS-CoV-2 antibody detected. Consistent with SARS-CoV-2 infection at some time.	May not correlate with functional immunity and does not exclude a possible re-infection
2	Not reactive	SARS-CoV-2 antibody not detected.	May not exclude recently acquired infections

9. References

For the information on the reference assessment grades given, refer to the [scientific information](#).

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