Medicines & Healthcare products Regulatory Agency

MHRA

Specification criteria for serology point of care tests and self-tests

Issued by MHRA

Version Control

1.0		Initial document

Introduction

These are initial specifications based on our best information, but the science is rapidly evolving. These specifications are subject to review and may need to be updated at short notice.

This is a specification of the minimally (and some preferred options) clinically acceptable specifications for point of care and self-tests to be made and used used in the UK during the current COVID-19 pandemic caused by SARS-CoV-2 virus. It sets out the clinical requirements based on the consensus of what is 'minimally acceptable' performance in the opinion of UK IVD industry, healthcare professionals and medical device regulators given the emergency situation. A test kit with lower specifications than this is likely to provide no clinical benefit and might lead to increased harm, which would be unacceptable.

Acceptable: Defines the minimum acceptable specification

Desired: Highly desirable features of considerable benefit. As time is of the essence if omitting one of these features significantly accelerates development and production it should be considered

Specification criteria for serology/antibody point of care test (POCT)		
These are initial specifications based on our best information, but the science is rapidly evolving. These specifications are subject to review and may need to be updated at short notice.		
Key Features	**Desired**	**Acceptable**
Priority Features		
Target Population The person providing the sample to be tested	People who need to know that they are immune to SARS CoV People may have recovered from suspected or confirmed SARS CoV 2 infection or they may have previously developed an asymptomatic infection.	
Target user setting The person operating the test kit	Health care professionals	Health care professionals
Intended Use	Detection of IgG antibodies to Sars-CoV-2 in venous or capillary blood, to assist screening for past SARS CoV 2 infection. Not suitable for diagnosing active infections	
Clinical sensitivity [a] (false negatives – telling someone they haven't had the infection when they have)	Greater than 98% (within 95% confidence intervals)	Greater than 98% (within 95% confidence intervals)
Clinical specificity (false positives - telling someone they have had the infection when they haven't)	Greater than 98% (within 95% confidence intervals) for IgG between 14 and 20 days from appearance of first symptoms	Greater than 98% (within 95% confidence intervals) for IgG between 14 and 20 days from appearance of first symptoms
Analytical specificity [b] (interferents and cross reactivity)	No cross reactivity with other coronaviruses	No cross reactivity with other coronaviruses
Type of analysis/result output	Qualitative	Qualitative/ Semi Quantitative
Sample type	Capillary whole blood from fingerstick sample OR Venous blood, serum or plasma	Capillary whole blood from fingerstick sample OR Venous blood, serum or plasma
Available Pack Size	Single/multiple packs	Single/multiple packs

Test Accessories	Pack includes all accessories needed for taking sample and its application to test	Accessories are routinely available in healthcare institution environment.
Regulatory status	CE Marked	CE marked
Ease of Use	• One signal test PLUS control • Easily interpreted by the intended user • No need for additional equipment to read result (eg camera, app etc)	• One signal PLUS control • Easily interpreted by the intended user • No need for additional equipment to read result (eg camera, app etc) • Operator is able to record results without having to write them manually

Test Procedure		
Number of steps to be performed by operator (incubation steps) [c]	No more than four steps For example • lance • apply blood • apply buffer • read	No more than five steps
Need for operator to transfer a precise volume of sample or reagents	No	Acceptable if robust transfer device is provided with the test device and if variation does not affect the test results
Requirement to add reagents e.g. sample diluent / buffer	No	Diluent provided in dropper bottle
Biosafety	No biosafety should be needed in addition to Personal Protective Equipment	No additional biosafety should be needed in addition to Personal Protective Equipment
Need for operator to transfer a precise volume of sample	No	No
Time to result	No more than 5 minutes	No more than 20 minutes

Internal control	Included, procedural control detecting the capability of the assay	Included, procedural control detecting the capability of the assay
Sample preparation Need to process sample prior to performing the test	No more than 15 minutes None or fully integrated	No more than 15 minutes None or fully integrated
Invalid rate	No more than 0.1%	No more than 1%

Operational characteristics		
Operating conditions	5 - 30°C 80% relative humidity	5 – 30°C 70% relative humidity
Reagent storage (shelf life stability)	12 months at 2- 35°C No cold chain required	12 months at 2- 35°C No cold chain required
In use stability	More than 1 hour after opening of an individual pouch	More than 30 minutes after opening of an individual pouch
Reagents reconstitution Need to prepare the reagents prior utilization	All reagents provided and ready to use	All liquids, including water, already in kit
End point stability (time window during which signal remains valid)	Up to 15 minutes	Up to 25 minutes
Reader to reader variation	More than 95% of readers should detect true positive results near the limit of detection	More than 95% of readers should detect true positive results near the limit of detection
Volume of sample	single drop for fingerstick tests	No more than two drops for fingerstick tests
Disposal requirements	None, device and accessories should be disposed in standard biological waste containers, no glassware Or be biodegradable or combustible.	None, device and accessories should be disposed in standard biological waste containers
Kit presentation (if not single format)	• 10 Test kit • Test components individually packed • Accessories not too small to be used with regular examination gloves • Include all required components and	• 5 Test kit • Test components individually packed • Accessories not too small to be used with regular examination gloves

	accessories to perform the test	
Training needs Time dedicated to training session for end users	None Job aid included in test kit	Minimal
Power Requirements	None required	None required
Need for Calibration/ maintenance/spare parts	None	None should be required
Instructions for Use	In line with IVDD (98/79/EC) Annex 1 requirements Simple interpretation by lay person with pictorials to aid sampling and results interpretation and what to do with the test if the control fails Clear reading time and Indications for different ranges of intensity/ concentration of target antigen/antibody Clear warnings of limitations for use including expected performance characteristic Paper or electronic	In line with IVDD (98/79/EC) Annex 1 requirements Simple interpretation by lay person with pictorials to aid sampling and results interpretation and what to do with the test if the control fails Clear reading time and Indications for different ranges of intensity/ concentration of target antigen/antibody Clear warnings of limitations for use including expected performance characteristic Paper or electronic
Manufacturing environment	Conforms to ISO 13485:2016	Conforms to ISO 13485:2016
Labelling and IFU	In accordance with Annex I of the IVD Directive under essential requirements	In accordance with Annex I of the IVD Directive under essential requirements
Lead time for production	1 month maximum	No more than 3 months

Specifications are subject to review and can be updated.

[a] Confirmation tests could be molecular PCR test for SARS CoV 2 virus using validated laboratory test on nasopharyngeal specimens

[b] Assessment of cross reactivity with other pathogens (prepandemic samples, other coronoavirus, SARS CoV 1, EBV, RF)

High priority organisms likely in the circulating area for example:

- Adenovirus (e.g. C1 Ad. 71)
- Human Metapneumovirus (hMPV)
- Parainfluenza virus 1-4
- Influenza A & B
- Enterovirus (e.g. EV68)
- Respiratory syncytial virus
- Rhinovirus
- Chlamydia pneumoniae
- Haemophilus influenzae
- Legionella pneumophila
- Mycobacterium tuberculosis
- Streptococcus pneumoniae
- Streptococcus pyogenes
- Bordetella pertussis
- Mycoplasma pneumoniae
- Pneumocystis jirovecii (PJP)

[c] Steps needed by operator e.g. preparation of reagents, lancing of finger for blood sample, adding sample to test cartridge, incubation time before reading.

Specification criteria for serology/antibody self-tests		
These are initial specifications based on our best information, but the science is rapidly evolving. These specifications are subject to review and may need to be updated at short notice.		
Key Features	**Desired**	**Acceptable**
Priority Features		
Target Population	People who need to know that they are immune to SARS CoV. People may have recovered from suspected or confirmed infection or they have previously developed an asymptomatic infection.	
Target user setting	No knowledge of self-testing technology	No knowledge of self-testing technology
Intended Use	Detection of IgG antibodies to Sars-CoV-2 in capillary blood, to assist screening for past SARS CoV 2 infection. Not suitable for diagnosing active infection.	

Clinical sensitivity [a] (false negatives – telling someone they haven't had the infection when they have)	Greater than 98% (within 95% confidence intervals)	Greater than 95% (within 95% confidence intervals)
Clinical specificity (false positives - telling someone they have had the infection when they haven't)	Greater than 98% (within 95% confidence intervals) for IgG between 14 and 20 days from appearance of first symptoms	Greater than 98% (within 95% confidence intervals) for IgG between 14 and 20 days from appearance of first symptoms
Analytical specificity [b] **(interferents and cross reactivity)**	No cross reactivity with other coronaviruses	No cross reactivity with other coronaviruses
Type of analysis/result output	Qualitative	Qualitative
Sample type	Capillary whole blood from fingerstick sample	Capillary whole blood from fingerstick sample
Available Pack Size	No more than two tests	Single test only
Test Accessories	Pack includes all accessories needed for taking sample and its application to test including lancet	
Regulatory status	CE Marked	CE marked
Ease of Use	• One signal test PLUS control • Easily interpreted by intended user • No need for additional equipment to read result (eg camera, app etc)	• One signal test PLUS control • Easily interpreted by intended user • No need for additional equipment to read result (eg camera, app etc)

Test procedure		
Number of steps to be performed by operator (incubation steps)[c]	No more than three steps For example • lance • apply blood • read	No more than four steps For example • lance • apply blood • apply buffer • read
Need for operator to transfer a precise volume of sample or reagents	No	A robust transfer device is provided with the test device. Volume variation does not affect the test results. Reagents do not offer additional risk to user.

Requirement to add reagents e.g. sample diluent / buffer	No	Diluent provided in dropper bottle
Biosafety	No biosafety should be required for self-testing or disposal of test/lancet	No biosafety should be required for self-testing or disposal of test/lancet
Need for operator to transfer a precise volume of sample	No	No
Time to result	No more than 5 minutes	No more than 20 minutes
Internal control	Included, procedural control detecting the capability of the assay	Included, procedural control detecting the capability of the assay
Sample preparation Need to process sample prior to performing the test	No more than 15 minutes None or fully integrated	No more than 15 minutes None or fully integrated
Invalid rate	<0.1%	<1%

Operational characteristics		
Operating conditions	5- 30°C 80% relative humidity	5 – 30°C 70% relative humidity
Reagent storage (stability)	12 months at 2- 35°C No cold chain required	12 months at 2- 35°C No cold chain required
In use stability	No more than 1 hour after opening of an individual pouch	No more than 30 minutes after opening of an individual pouch
Reagents reconstitution Need to prepare the reagents prior utilization	All reagents provided and ready to use	All liquids, including water, already in kit
End point stability (time window during which signal remains valid)	Up to 15 minutes	Up to 25 minutes
Reader to reader variation	More than 95% of readers should detect positive results near the limit of detection	More than 95% of readers should detect positive results near the limit of detection
Volume of sample	Single drop for fingerstick tests	No more than two drops
Disposal requirements	None Dispose in household waste	None Dispose in household waste
Kit presentation	• Test components individually packed	• Test components individually packed

	• Accessories not too small to be used with regular examination gloves Include all required components and accessories to perform the test	• Accessories not too small to be used with regular examination gloves
Training needs Time dedicated to training session for end users	None	None
Power Requirements	None should be required	None should be required
Need for Calibration/ maintenance/spare parts	None	None should be needed
Instructions for Use	In line with annex I requirements Simple interpretation by lay person with pictorials to aid sampling and results interpretation Clear reading time and Indications for different ranges of intensity/ concentration of target antibody Clear warnings of limitations for use Paper	In line with annex I requirements Simple interpretation by lay person with pictorials to aid sampling and results interpretation Clear reading time and Indications for different ranges of intensity/ concentration of target antibody Clear warnings of limitations for use Paper
Manufacturing environment	Conforms to ISO 13485 2016	Conforms to ISO 13485 2016
Labelling and IFU	In accordance with Annex I of the 98/79/EC IVD Directive under essential requirements	In accordance with Annex I of the 98/79/EC IVD Directive under essential requirements
Lead time for production	1 month maximum	<3 months

Specifications are subject to review and can be updated.

[a] Confirmation tests could be molecular PCR test for SARS CoV 2 virus using validated laboratory test on nasopharyngeal specimens

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- Streptococcus pyogenes
- Bordetella pertussis
- Mycoplasma pneumoniae
- Pneumocystis jirovecii (PJP)

[c] Steps needed by operator e.g. preparation of reagents, lancing of finger for blood sample, adding sample to test cartridge, incubation time before reading.

Glossary

Point of care test
An *in vitro* diagnostic medical device intended to be used by a healthcare professional outside of a laboratory in primary or secondary care environments

Self-test
An *in vitro* diagnostic medical device intended to be used by a lay person on a home environment

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