ACON Laboratories, Inc.

SARS-CoV-2 Antigen Rapid Test

- Convenient nasal swab specimens
- Fast results in 15 minutes
- Excellent performance compared to molecular PCR methods
- Room temperature storage

The Flow*flex* SARS-CoV-2 Antigen Rapid Test is a lateral flow chromatographic immunoassay for the qualitative detection of the nucleocapsid protein antigen from SARS-CoV-2 in nasal swab specimens directly from individuals who are suspected of an active COVID-19 infection by their healthcare provider within the first seven days of the onset of symptoms.

Clinical Performance

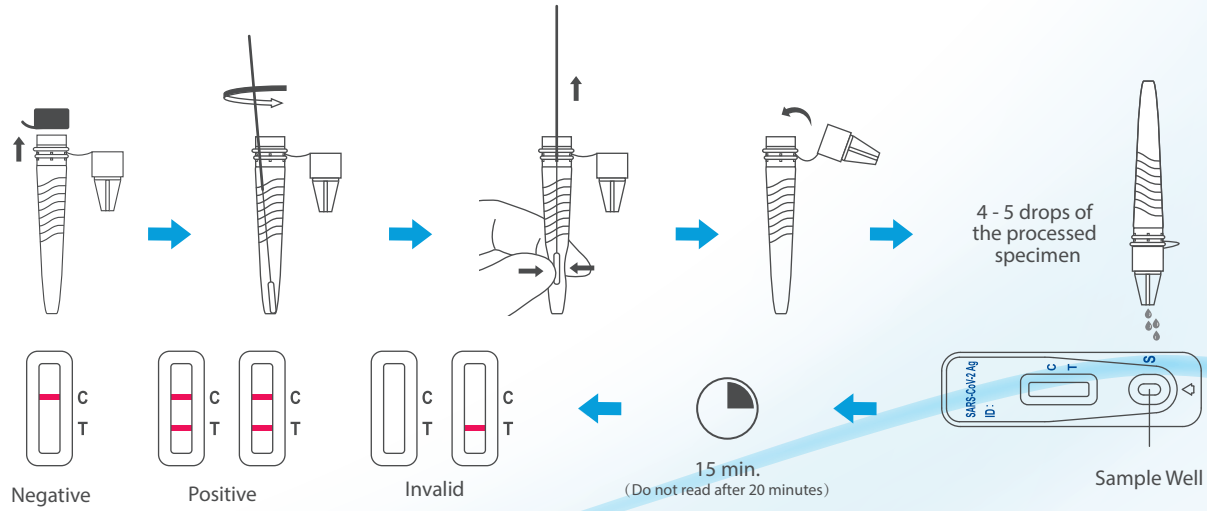
The performance of Flow*flex* SARS-CoV-2 Antigen Rapid Test was established with 304 nasal swabs collected from individual symptomatic patients (within 7 days of onset) who were suspected of COVID-19. The performance of the Flow*flex* SARS-CoV-2 Antigen Rapid Test was compared to a RT-PCR method.

Clinical Performance of SARS-CoV-2 Antigen Rapid Test

Method		RT-PCR		Total Results
SARS-CoV-2 Antigen Rapid Test	Results	Negative	Positive	
	Negative	269	1	270
	Positive	1	33	34
Total Results		270	34	304

Sensitivity: 97.1% (83.8% - 99.9%)* Specificity : 99.6% (97.7% - 99.9%)* Accuracy : 99.3% (97.5% - 99.9%)*

Test Procedure and Interpretation



Ordering Information

Product Name	Catalog No.	Format	Specimen	Package
Flow*flex* SARS-CoV-2 Antigen Rapid Test	L031-11815	Cassette	Nasal swabs	25 Tests/Kit

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CE

Flowflex™

SARS-CoV-2 Antigen Rapid Test
Package Insert

REF L031-11815	English

A rapid test for the qualitative detection of SARS-CoV-2 nucleocapsid antigens in nasal swab specimens.
For professional in vitro diagnostic use only.

INTENDED USE

The SARS-CoV-2 Antigen Rapid Test is a lateral flow chromatographic immunoassay for the qualitative detection the nucleocapsid protein antigen from SARS-CoV-2 in nasal swab specimens directly from individuals who are suspected of COVID-19 by their healthcare provider within the first seven days of the onset of symptoms. The SARS-CoV-2 Antigen Rapid Test does not differentiate between SARS-CoV and SARS-CoV-2.

Results are for the identification of SARS-CoV-2 nucleocapsid antigen. This antigen is generally detectable in upper respiratory samples during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease.

Negative results, from patients with symptom beyond seven days, should be treated as presumptive and confirmed with a molecular assay, if necessary, for patient management. Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions. Negative results should be considered in the context of a patient's recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19.

The SARS-CoV-2 Antigen Rapid Test is intended for use by trained clinical laboratory personnel and individuals trained in point of care settings. SARS-CoV-2 Antigen Rapid Test is intended to be used as an aid in the diagnosis of SARS-CoV-2 infection.

SUMMARY

The novel coronaviruses belong to the β genus.[1] COVID-19 is an acute respiratory infectious disease. People are generally susceptible. Currently, the patients infected by the novel coronavirus are the main source of infection; asymptomatic infected people can also be an infectious source. Based on the current epidemiological investigation, the incubation period is 1 to 14 days, mostly 3 to 7 days. The main manifestations include fever, fatigue and dry cough. Nasal congestion, runny nose, sore throat, myalgia and diarrhea are found in a few cases.

PRINCIPLE

The SARS-CoV-2 Antigen Rapid Test is a qualitative membrane based chromatographic immunoassay for the qualitative detection of the nucleocapsid protein antigen from SARS-CoV-2 in human nasal swab specimens.

When specimens are processed and added to the test cassette, SARS-CoV-2 antigens, if present in the specimen, will react with the anti-SARS-CoV-2 antibody-coated particles, which have been pre-coated on the test strip. The mixture then migrates upward on the membrane by capillary action. The antigen-conjugate complexes migrate across the test strip to the reaction area and are captured by a line of antibody bound on the membrane. Test results are interpreted visually at 15-30 minutes based on the presence or absence of visually colored lines.

To serve as a procedure control, a colored line will always appear in the control line region indicating that proper volume of specimen has been added and membrane wicking has occurred.

REAGENTS

The test cassette contains anti-SARS-CoV-2 antibodies. The positive control swab contains SARS-CoV-2 recombinant antigen pre-coated on the swab.

PRECAUTIONS

- For professional *in vitro* diagnostic use only. Do not use after the expiration date.
- Do not eat, drink, or smoke in the area where the specimens or kits are handled.
- Do not use the test if the pouch is damaged.
- Handle all specimens as if they contain infectious agents. Observe established precautions against biological hazards throughout testing and follow the standard procedures for proper disposal of specimens.
- Wear protective clothing such as laboratory coats, disposable gloves, mask and eye protection when specimens are being tested.
- The used test should be discarded according to local regulations. The used test should be considered potentially infectious and be discarded according to local regulations.
- Humidity and temperature can adversely affect results.
- This package insert must be read completely before performing the test. Failure to follow directions in insert may yield inaccurate test results.
- The test line for a high viral load sample may become visible within 15 minutes, or as soon as the sample passes the test line region.
- The test line for a low viral load sample may become visible within 30 minutes.

STORAGE AND STABILITY

- The kit can be stored at temperatures between 2 - 30 °C.
- The test is stable until the expiration date printed on the sealed pouch.
- The test must remain in the sealed pouch until use.
- DO NOT FREEZE.
- Do not use after the expiration date.

MATERIALS

Materials Provided

- Test Cassettes
- Positive Control Swab
- Disposable Swabs*
- Extraction Buffer Tubes
- Negative Control Swab
- Package Insert

* *The Disposable Swabs are produced by another manufacturer.*

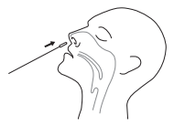
Materials Required But Not Provided

- Personal Protective Equipment
- Timer

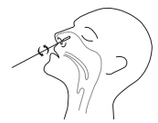
SPECIMEN COLLECTION AND PREPARATION

- The SARS-CoV-2 Antigen Rapid Test can be performed using nasal swab specimens.
- Testing should be performed immediately after specimen collection, or at most within one (1) hour after specimen collection, if stored at room temperature (15-30°C).
- To collect a nasal swab sample:

1. Carefully insert a Disposable Swab, **provided with your kit**, into one nostril. Using gentle rotation, push the swab up to 2.5 cm (1 inch) from the edge of the nostril.



2. Rotate the swab 5 times against the mucosa inside the nostril to ensure sufficient specimen collection.



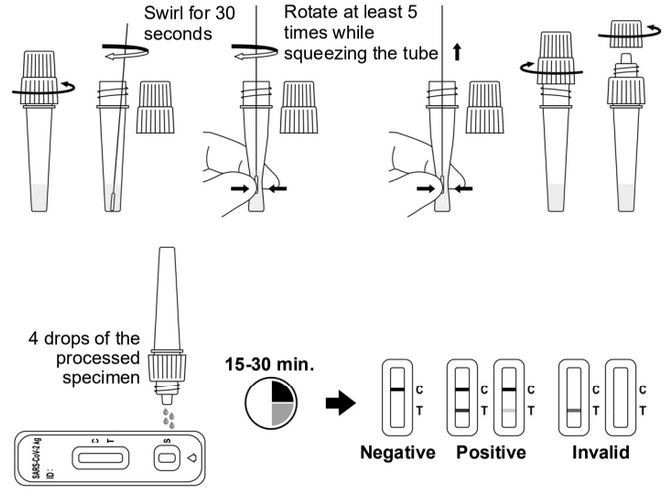
3. Using the same swab, repeat this process in the other nostril to ensure that an adequate amount of sample is collected from both nasal cavities.

4. Withdraw the swab from the nasal cavity. The specimen is now ready for preparation using the extraction buffer tubes.

DIRECTIONS FOR USE

Allow the test and extraction buffer to reach room temperature (15-30 °C) prior to testing.

1. Use an extraction buffer tube for each specimen to be tested and label each tube appropriately.
2. Unscrew the dropper cap from the extraction buffer tube without squeezing.
3. Insert the swab into the tube and swirl it for 30 seconds. Then rotate the swab at least 5 times while squeezing the sides of the tube. Take care to avoid splashing contents out of the tube.
4. Remove the swab while squeezing the sides of the tube to extract the liquid from the swab.
5. Screw the dropper cap firmly onto the extraction buffer tube containing the sample. Mix thoroughly by swirling or flicking the bottom of the tube.
6. Remove the test cassette from the foil pouch and use it as soon as possible.
7. Place the test cassette on a flat and clean surface.
8. Add the processed specimen to the sample well of the test cassette.
   a. Unscrew the small cap from the dropper tip.
   b. Invert the extraction buffer tube with the dropper tip pointing downwards and hold it vertically.
   c. Gently squeeze the tube, dispensing 4 drops of the processed specimen into the sample well.
9. Wait for the colored line(s) to appear. The result should be read at 15-30 minutes. **Do not read the result after 30 minutes.**



INTERPRETATION OF RESULTS

(Please refer to the illustration above)

NEGATIVE: Only one colored control line appears in the control region (C). No apparent colored line appears in the test line region (T). This means that no SARS-CoV-2 antigen was detected.

POSITIVE:* Two distinct colored lines appear. One line in the control line region (C) and the other line-in the test line region (T). This means that the presence of SARS-CoV-2 antigen was detected.

***NOTE:** The intensity of the color in the test line (T) may vary depending on the level of the SARS-CoV-2 antigen present in the specimen. Therefore, any shade of color in the test line region (T) should be considered positive.

INVALID: Control line fails to appear. Insufficient specimen volume or incorrect operation are the most likely reasons for control line failure. Review the procedure and repeat the test with a new test cassette. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

QUALITY CONTROL

Internal procedural controls are included in the test. A colored line appearing in the control line region (C) is an internal procedural control. It confirms sufficient specimen volume and correct procedural technique.

Positive and Negative control swabs are supplied with each kit. These control swabs should be used to ensure that the test cassette and that the test procedure is performed correctly. Follow the "**DIRECTIONS FOR USE**" section to perform the control test.

The control swabs can be tested under any of the following circumstances:

1. When new lot of tests are used and/or when a new operator performs the test.
2. At periodic intervals as dictated by local requirements, and/or by the user's Quality Control procedures.

LIMITATIONS

1. The SARS-CoV-2 Antigen Rapid Test is for *in vitro* diagnostic use only. The test should be used for the detection of SARS-CoV-2 antigens in nasal swab specimens only. The intensity of the test line does not necessarily correlate to SARS-CoV-2 viral titer in the specimen.
2. Specimens should be tested as quickly as possible after specimen collection and at most within the hour following collection.
3. Use of viral transport media may result in decreased test sensitivity.
4. A false-negative test may result if the level of antigen in a sample is below the detection limit of the test or if the sample was collected incorrectly.
5. Test results should be correlated with other clinical data available to the physician.
6. A positive test result does not rule out co-infections with other pathogens.
7. A positive test result does not differentiate between SARS-CoV and SARS-CoV-2.
8. A negative test result is not intended to rule out other viral or bacterial infections.
9. A negative result, from a patient with symptom onset beyond seven days, should be treated as presumptive and confirmed with a molecular assay, if necessary, for clinical management.
   (If the differentiation of specific SARS viruses and strains is needed, additional testing is required.)

PERFORMANCE CHARACTERISTICS

Clinical Sensitivity, Specificity and Accuracy

The performance of SARS-CoV-2 Antigen Rapid Test was established with 605 nasal swabs collected from individual symptomatic patients who were suspected of COVID-19. The results show that the relative sensitivity and the relative specificity are as follows:

Clinical Performance for SARS-CoV-2 Antigen Rapid Test

Method		RT-PCR		Total Results
SARS-CoV-2 Antigen Rapid Test	Results	Negative	Positive	
	Negative	433	5	438
	Positive	2	165	167
Total Results		435	170	605

Relative Sensitivity: 97.1% (93.1%-98.9%)* Relative Specificity: 99.5% (98.2%-99.9%)*

Accuracy: 98.8% (97.6%-99.5%)* *95% Confidence Intervals

Stratification of the positive samples post onset of symptoms between 0-3 days has a positive percent agreement (PPA) of 98.8% (n=81) and 4-7 days has a PPA of 96.8% (n=62).

Positive samples with Ct value ⩽33 has a higher positive percent agreement (PPA) of 98.7% (n=153) .

Limit of Detection (LOD)

The LOD of SARS-CoV-2 Antigen Rapid Test was established using limiting dilutions of an inactivated viral sample. The viral sample was spiked with negative human nasal sample pool into a seral of concentrations. Each level was tested for 30 replicates. The results show that the LOD is $1.6*10^2$ $TCID_{50}$/mL.

Sample SARS-CoV-2 Concentration	% Positive (Tests)
$1.28*10^3$ $TCID_{50}$/mL	100% (30/30)
$6.4*10^2$ $TCID_{50}$/mL	100% (30/30)
$3.2*10^2$ $TCID_{50}$/mL	100% (30/30)
$1.6*10^2$ $TCID_{50}$/mL	96.7% (29/30)
$8*10$ $TCID_{50}$/mL	0% (0/30)

Cross-Reactivity (Analytical Specificity) and Microbial Interference

Cross-reactivity was evaluated by testing a panel of related pathogens and microorganisms that are likely to be present in the nasal cavity. Each organism and virus were tested in the absence or presence of heat-inactivated SARS-CoV-2 virus at low positive level.

No cross-reactivity or interference was observed with the following microorganisms when tested at the concentration presented in the table below. The SARS-CoV-2 Antigen Rapid Test does not differentiate between SARS-CoV and SARS-CoV-2.

Potential Cross-Reactant		Test Concentration	Cross-Reactivity (in the absence of SARS-CoV-2 virus)	Interference (in the presence of SARS-CoV-2 virus)
Virus	Adenovirus	1.14×10^6 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Enterovirus	9.50×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Human coronavirus 229E	1.04×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Human coronavirus OC43	2.63×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Human coronavirus NL63	1.0×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Human Metapneumovirus	1.25×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	MERS-coronavirus	7.90×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Influenza A	1.04×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Influenza B	1.04×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Parainfluenza virus 1	1.25×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Parainfluenza virus 2	3.78×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Parainfluenza virus 3	1.0×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Parainfluenza virus 4	2.88×10^6 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Respiratory syncytial virus	3.15×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Rhinovirus	3.15×10^5 $TCID_{50}$/mL	No 3/3 negative	No 3/3 positive
	Human coronavirus-HKU1	1×10^5 copies/mL	No 3/3 negative	No 3/3 positive
Bacteria	Bordetella pertussis	2.83×10^9 CFU/mL	No 3/3 negative	No 3/3 positive
	Chlamydia trachomatis	3.13×10^8 CFU/mL	No 3/3 negative	No 3/3 positive
	Haemophilus influenza	1.36×10^8 CFU/mL	No 3/3 negative	No 3/3 positive
	Legionella pneumophila	4.08×10^9 CFU/mL	No 3/3 negative	No 3/3 positive
	Mycobacterium tuberculosis	1.72×10^7 CFU/mL	No 3/3 negative	No 3/3 positive
	Mycoplasma pneumoniae	7.90×10^7 CFU/mL	No 3/3 negative	No 3/3 positive
	Staphylococcus aureus	1.38×10^7 CFU/mL	No 3/3 negative	No 3/3 positive
	Staphylococcus epidermidis	2.32×10^9 CFU/mL	No 3/3 negative	No 3/3 positive
	Streptococcus pneumoniae	1.04×10^8 CFU/mL	No 3/3 negative	No 3/3 positive
	Streptococcus pyogenes	4.10×10^6 CFU/mL	No 3/3 negative	No 3/3 positive
	Pneumocystis jirovecii-S. cerevisiae	8.63×10^7 CFU/mL	No 3/3 negative	No 3/3 positive
	Pseudomonas aeruginosa	1.87×10^8 CFU/mL	No 3/3 negative	No 3/3 positive
	Chlamydia pneumoniae	1×10^6 IFU/ml	No 3/3 negative	No 3/3 positive
Yeast	Candida albicans	1.57×10^8 CFU/mL	No 3/3 negative	No 3/3 positive
Pooled human nasal wash			No 3/3 negative	No 3/3 positive

Interfering Substances

The following substances, naturally present in respiratory specimens or that may be artificially introduced into the nasal cavity or nasopharynx, were evaluated. Each substance was tested in the absence or presence of SARS-CoV-2 virus at low positive level. The final concentration of the substances tested are listed below and were found not to affect test performance.

Interfering Substance	Active Ingredient	Concentration	Results (in the absence of SARS-CoV-2 virus)	Results (in the presence of SARS-CoV-2 virus)
Endogenous	Biotin	2.4 mg/mL	3/3 negative	3/3 positive
	Mucin	0.5% w/v	3/3 negative	3/3 positive
	Whole Blood	4% v/v	3/3 negative	3/3 positive
Afrin Original Nasal Spray	Oxymetazoline	15% v/v	3/3 negative	3/3 positive
ALKALOL Allergy Relief Nasal Spray	Homeopathic	1:10 Dilution	3/3 negative	3/3 positive
Chloraseptic Max Sore Throat Lozenges	Menthol, Benzocaine	1.5 mg/mL	3/3 negative	3/3 positive
CVS Health Fluticasone Propionate Nasal Spray	Fluticasone propionate	5% v/v	3/3 negative	3/3 positive
Equate Fast-Acting Nasal Spray	Phenylephrine	15% v/v	3/3 negative	3/3 positive
Equate Sore Throat Phenol Oral Anesthetic Spray	Phenol	15% v/v	3/3 negative	3/3 positive
Original Extra Strong Menthol Cough Lozenges	Menthol	1.5 mg/mL	3/3 negative	3/3 positive
NasalCrom Nasal Spray	Cromolyn	15% v/v	3/3 negative	3/3 positive
NeilMed NasoGel for Dry Noses	Sodium Hyaluronate	5% v/v	3/3 negative	3/3 positive
Throat Lozenge	Dyclonine Hydrochloride	1.5mg/mL	3/3 negative	3/3 positive
Zicam Cold Remedy	Galphimia glauca, Luffa operculata, Sabadilla	5% v/v	3/3 negative	3/3 positive
Antibiotic	Mupirocin	10 mg/mL	3/3 negative	3/3 positive
Tamiflu	Oseltamivir Phosphate	5 mg/mL	3/3 negative	3/3 positive
Antibiotic	Tobramycin	4 µg/mL	3/3 negative	3/3 positive
Mometasone Furoate Nasal Spray	Mometasone Furoate	5%v/v	3/3 negative	3/3 positive
Physiological Seawater Nasal Cleaner	NaCl	15%v/v	3/3 negative	3/3 positive

PRECISION

Intra-Assay

Within-run precision was determined using 60 replicates of specimens: negative control and SARS-CoV-2 antigen positive controls. The specimens were correctly identified >99% of the time.

Inter-Assay

Between-run precision was determined using 60 independent assays on the same specimen: negative specimen and SARS-CoV-2 antigen positive specimen. Three different lots of the SARS-CoV-2 Antigen Rapid Test were tested using these specimens. The specimens were correctly identified >99% of the time.

BIBLIOGRAPHY

1. Shuo Su, Gary Wong, Weifeng Shi, et al. Epidemiology, Genetic recombination, and pathogenesis of coronaviruses. Trends in Microbiology, June 2016, vol. 24, No. 6: 490-502
2. Susan R. Weiss, Julian L. Leibowitz, Coronavirus Pathogenesis, Advances in Virus Research, Volume 81: 85-164

Index of Symbols

	Manufacturer	Σ	Contains sufficient for <*n*> tests		Temperature limit
IVD	*In vitro* diagnostic medical device		Use-by date		Do not reuse
	Consult instructions for use	LOT	Batch code	REF	Catalogue number
EC REP	Authorized representative in the European Community				Date of manufacture

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SARS-CoV-2 Antigen Rapid Test	SARS-CoV-2 Antigen Rapid Test

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EC REP
MedNet GmbH
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48163 Muenster, Germany

Number: 1151255504
Effective date: 2020-12-20

Flowflex Rapid Antigen Tests – FAQ's

Where are the tests made?

Acon is a large global diagnostics company. They are based in the US with manufacturing facilities in the US, China and Mexico. The factory in China has been inspected and approved by the FDA.

It is very important to us that we know exactly where our tests are made and by whom to ensure consistency of quality and supply.

Are they approved for use in the UK & Ireland?

All medical devises have to follow a standard process before they can be sold in the EU. These tests have been through that process and have a CE mark. They can be sold and used in the UK & Ireland within their intended use.

Are they approved by the MHRA?

The MHRA is the competent authority or regulatory body in the UK. They do not approve tests other than to allow the manufacturers to put a CE mark on the product. The MHRA did, however, produce a target product profile that contains criteria that tests should meet. The Flowflex rapid antigen tests meet all of the target profile.

Are they approved by Public Health England?

Public Health England have been assessing tests in the UK at their labs in Porton Down. Although Flowflex has been submitted for review, it has not yet been called up for evaluation. As and when this happens we will advise our customers.

When should the tests be used?

The Flowflex tests pick up moderate to high viral loads. Patients will have moderate to high viral loads about 3 days before symptoms start until between 7 and 10 days after symptoms start. In this window lateral flow tests, such as Flowflex are very effective. A positive test should be repeated using a RT-PCR test for confirmation and entry into the national test and trace system. A negative test simply reflects a point in time – you do not have active COVID-19 today.

How often should tests be repeated?

This is difficult to advise as advice differs. Bear in mind that a negative result reflects a moment in time. Some bodies have advised testing twice a week, or perhaps every Monday in a standard five day week. Other guidance has suggested testing every day.

What is the regulatory status of the Flowflex tests?

The pack clearly states, 'For professional in vitro diagnostic use only'. We take that to mean that all testing should be under the supervision of a healthcare professional. How that supervision should be carried out is a grey area. We know, for example, in schools non-health professional staff receive on line training and are then allowed to carry out the tests. We also know of groups that test multiple people within a single zoom meeting.

One thing is certain; lateral flow antigen tests are not to be sold direct to the public for self-testing. That would require another level of approval. At this stage there isn't a lateral flow antigen test on the market that is approved test has been approved for self-testing.

Flowflex™

How can I make a test to be as effective as possible?

The testing process is very simple, however, a few minor things may cause issues in test accuracy.

Snot – if the patient is very snotty then taking large amounts of snot can thicken the buffer and make it slower to travel along the test cassette. Ask the patient to blow their nose.

Buffer – make sure that the buffer is in the bottom of the tube before taking off the lid. Give it a little flick before. Make sure that you squeeze the walls of the tube around the swab to extract all of the sample and again flick the side of the tube before applying the sample into the sample well.

Test cassette – make sure that it is on a flat level surface.

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