COVID-19: OPERATIONAL FRAMEWORK FOR THE DEPLOYMENT OF ANTIGEN DIAGNOSTIC TESTS FOR SARS-COV-2

Version 1.0

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Version	Date Approved	Changes	Author
1.0	29.01.21	First draft	ADT Validation Scientific Lead ADT Implementation Project Manager

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1.0 Glossary

#	Term	Description
1	**ADT**	Antigen Diagnostic Tests
2	**CCT**	Covid Care Tracker
3	**CIDR**	Computerised Infectious Disease Reporting System
4	**Swiftqueue**	Software for scheduling appointments
5	**HPSC**	Health Protection Surveillance Centre
6	**LIMS**	Laboratory Information Management System
7	**NPT**	Near-Patient Testing
8	**NPHET**	National Public Health Emergency Team
9	**PCR**	Polymerase Chain Reaction
10	**PH**	Public Health
11	**PPE**	Personal Protective Equipment
12	**WHO**	Word Health Organisation

2.0 Background

To date, testing for SARS-CoV-2 infection has mostly relied on reverse transcription polymerase chain reaction (RT-PCR) performed on a nasopharyngeal or deep-nasal/mid-turbinate specimens. This testing method remains the gold standard for detecting SARS-CoV-2.

Following approval by the National Public Health Emergency Team (NPHET) for the use of Antigen Diagnostic Tests (ADT) in certain settings, ADT will be deployed to support the pandemic response.

See HPSC: Interim guidance on use of Antigen Detection Tests in the public health system in Ireland which outlines settings approved for use for ADT.

3.0 Purpose

This document is intended to provide assistance for users of ADT in the performance of testing, and to act as an overarching operational framework that should guide the use of ADT in a near-patient test (NPT) setting.

ADT users will be required to apply clinical and scientific expertise to ensure that ADT is used in each setting in ways that are safe for those who perform the testing and those who are tested, and that provide an effective quality assured service. This requires clear clinical governance and accountability that includes not only performance, but also interpretation and communication of results.

4.0 Scope

This operational framework covers all aspects of ADT. This ranges from the point of sampling an individual to the performance of ADT, and subsequent recording and reporting of detected results.

As laboratory based ADT have not concluded validation, this document covers near-patient testing ADT and will be updated in due course.

5.0 Target users

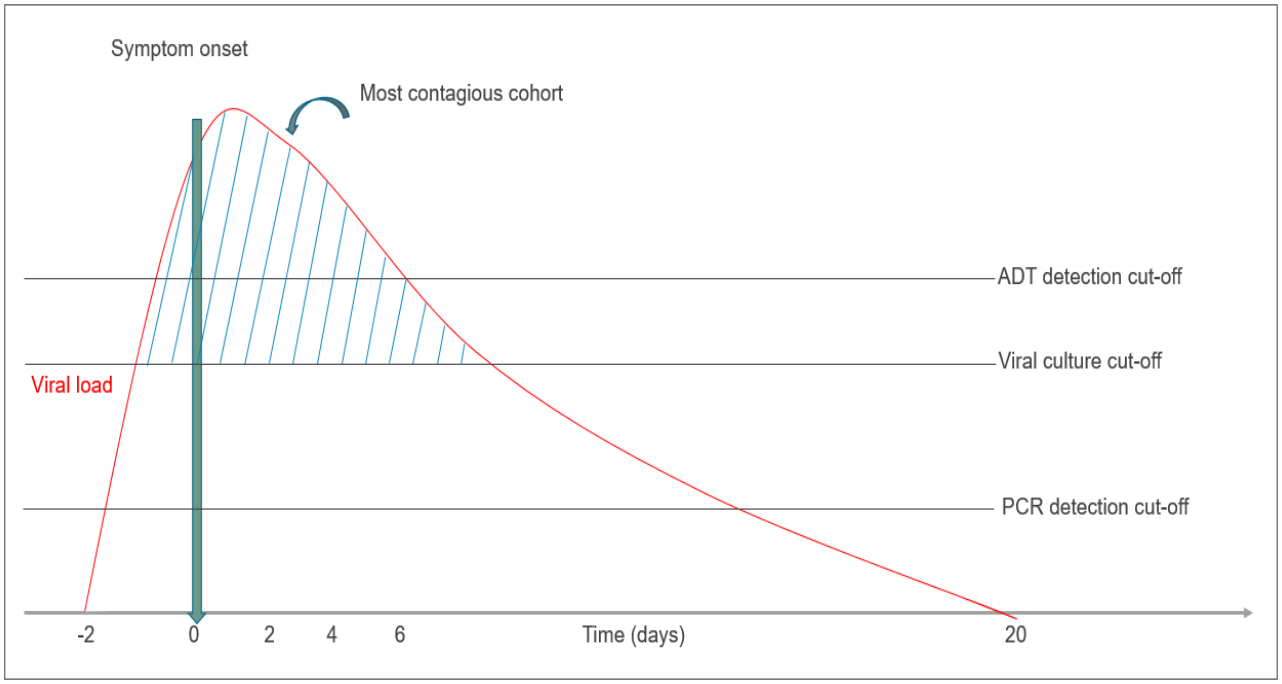
All users of ADT approved by the HSE.

6.0 Objective

The objective of this operational framework is to ensure correct use of ADT and consistency in the completion of operational requirements.

7.0 Antigen Diagnostic Tests

ADT are comparatively easy to use and offer rapid results. Correctly applied ADT may offer benefits in comparison to RT-PCR tests for the diagnostic of SARS-CoV-2 in certain contexts, although completion of ADT can be considered labour intensive. They have been developed as both laboratory-based tests and for NPT, and results are normally generated in 10 to 30 minutes after the start of the analysis, and at lower cost for supplies compared with RT-PCR. However, available ADT have demonstrated lower sensitivity when compared to the gold standard RT-PCR test, while their specificity is generally reported to be high. Furthermore, their intended use is in symptomatic patients within the first 5 days of symptom onset when viral loads are highest as outlined in the below graph.



8.0 Clinical Governance

In any acute setting under the HSE where ADT is deployed, the clinical director of diagnostics will be responsible for overall clinical governance with input from a clinical microbiology.

In the community, the testing is ordered by Public Health, as a response to an outbreak, and governance of who is to be tested, informing patients, and advising on actions based on the results rests with Public Health and the outbreak control team. Governance of undertaking the tests in a supervised manner, and in a quality management system rests with the NAS working with the local Clinical Microbiologist.

9.0 Roles and Responsibilities

The following roles and responsibilities will be required at a minimum when performing ADT. These requirements may differ depending on the specific setting.

Role	Responsibilities
Clinical Director of the Laboratory/ Diagnostic Service	• Professionally accountable for the quality of the results reported.
Administration	• Supports coordination of workflow at testing site, organising test materials, paperwork, labelling, and scheduling. • Collects ADT testing information and clinical data from individuals to enable reporting (e.g. ADT batch/lot numbers, demographics, symptoms, results). • Monitors activity. • Supports the testing centre staff in carrying out the additional sampling tasks required. • Schedules the walk in individuals as required.
Swabbing	• Explains the swabbing procedure to the individual and the details of what is required. • Collects the test samples from the individual in line with training. • Adheres to all requirements associated with assuring infection control procedures are carried out.
Testing	• Receives samples from the test operator (‘the ‘swabber’) and performs ADT. • Interprets ADT results.
Review and authorisation	• Undertakes the process for review of testing information captured (e.g. patient information) and authorisation of results.
Quality assurance	• Batch acceptance of reagents and traceability. • Ensures appropriate EQA and IQC processes are implemented and maintained.
Communication of positive results	• Contacts the individual(s) with a detected (positive) ADT immediately, informing them of their result and requesting them to isolate.
Reporting	• Records results on ADT result template. • Ensures positive results are notified to required individuals and stakeholders. • Updates required systems (where necessary) with results for onward Public Health management including contact tracing and surveillance. • Ensures public health is provided with all results and testing activity.

10.0 Procedures in Antigen Testing

10.1 Health and Safety Processes

The Safety, Health and Welfare at Work (Biological Agents) Regulations 2013 (S.I. No. 572 of 2013) article 16, documents the special measures required for working with biological agents in health care setting other than diagnostic laboratories. Before commencing any SARS-CoV-2 ADT, a full risk assessment should be completed. Sites should utilise their own risk assessment template when completing this step or refer to the HSE Risk Assessment Template available on the Quality Assurance and Verification Division of the HSE website.

The risk assessment should consider the following:

- Who is being tested?
- Who is taking the samples and carrying out testing?
- Have they completed ADT training and passed the competency assessment?
- What type of samples are being taken (nature of the sample)?
- Where are the samples being taken?
- Where is the test being carried out?
- How are samples and any waste disposed of?
- Are there other people who may be affected by work activity? (E.g. pregnant employees, people handling the waste, cleaners etc.?)
- Are there appropriate decontamination and disinfection procedures in place?

In conducting the risk assessment account should be taken of WHO guidance and HPSC public health guidance.

10.1.1 Personal Protective Equipment

Before commencing any sampling or testing for SARS-CoV-2, the appropriate PPE must be put on (Table 1). Please refer to HSE guidelines for donning and doffing PPE.

- COVID - 19 Safe PPE – Care of Patients with respiratory symptoms/ suspected/ confirmed COVID -19 - 30/04/20
- Safe use of Masks – 26/08/20
- Putting on (donning) Personal Protective Equipment (PPE) - 19/05/20
- Taking Off (doffing) Personal Protective Equipment (PPE) - 27/07/20
- Doffing gowns in the context of COVID -19 – 06/11/20

Table 1: PPE requirements for procedures in ADT testing

Procedure	Personal Protective Equipment
Sample collection	• Alcohol hand rub • Non-sterile gloves; single-use only • Gown; long sleeved fluid repellant • Eye protection (safety glasses or goggles, face-shields [visors]) if there is a risk of splash • Surgical mask (use of a respirator mask may be considered instead of a surgical mask based on risk assessment)
Sample receipt and accession	• Alcohol hand rub • Non-sterile gloves; single-use only • Gown; long sleeved fluid repellant • Surgical mask (use of a respirator mask may be considered instead of a surgical mask based on risk assessment)
ADT sample testing	• Alcohol hand rub • Non-sterile gloves; single-use only • Gown; long sleeved, fluid repellent • Eye protection (safety glasses or goggles, face-shields [visors]) • Respirator. e.g. N95, FFP2

10.1.2 Waste Management

The following procedure applies to ADT samples only:

1. Handle all waste from sample collection and SARS-CoV-2 ADT testing as biohazardous.
2. Disposal of SARS-CoV-2 ADT used cassettes:
    a. Read manufacturer's specific instructions.
    b. Read Material Safety Data Sheets.
    c. As per local guidelines, used cassettes should be disposed of in biohazard bins.
3. All components of SARS-CoV-2 ADTs are single-use and must not be reused.
4. Place all contaminated materials (such as used sample containers) in biohazard bins.

10.1.3 Procedure for cleaning up spills

The following procedure applies to ADT samples only:

1. Flood the spill area with 1% bleach.
2. Cover the spill and disinfectant with paper towel.
3. Leave for at least 10 minutes.
4. Wipe up the spill and disinfectant with paper towel and discard in the biohazard waste container.
5. Disinfect the area with 1% bleach or 70% alcohol and dry with paper towel. Discard the paper towel in the biohazard waste container.

10.2 Setup of Workstation

ADT must be performed on a designated well-ventilated bench, separate from the sample collection area and other areas where patients have access.

The work area should be marked with a biohazard sign and accessible only to staff who have been trained and are conducting the testing.

The workstation should be set up with dirty and clean areas, ensuring adequate space on both as indicated below.

All contaminated materials (such as sample containers, transfer pipettes, tubes and cassettes) must be disposed of in a yellow biohazard bin.

Waste disposal bins must have sufficient absorbent material in the base to absorb all liquid – it's best to assume that all contents leak, and to act accordingly to ensure there is enough material to absorb any and all liquid.

10.2.1 Requirements:

Dirty Area

- Non-porous work surface, suitable for wiping down
- Hard Clinical Waste Bin (Yellow - adjustable closure)
- Clinical Waste leak proof Bag and Biohazard bin (both Yellow)
- Supply of disposable gloves (size appropriate)
- Timers
- Disinfection products
    - Surface: Chloros 1:100; alcohol 70%
    - Hand: hand sanitiser
- Paper towels
- Absorbent pads/ a contained plastic tray
- ADT test kit
- Rack for samples
- Waterproof markers
- Instructions for Use - Laminated

Clean Area

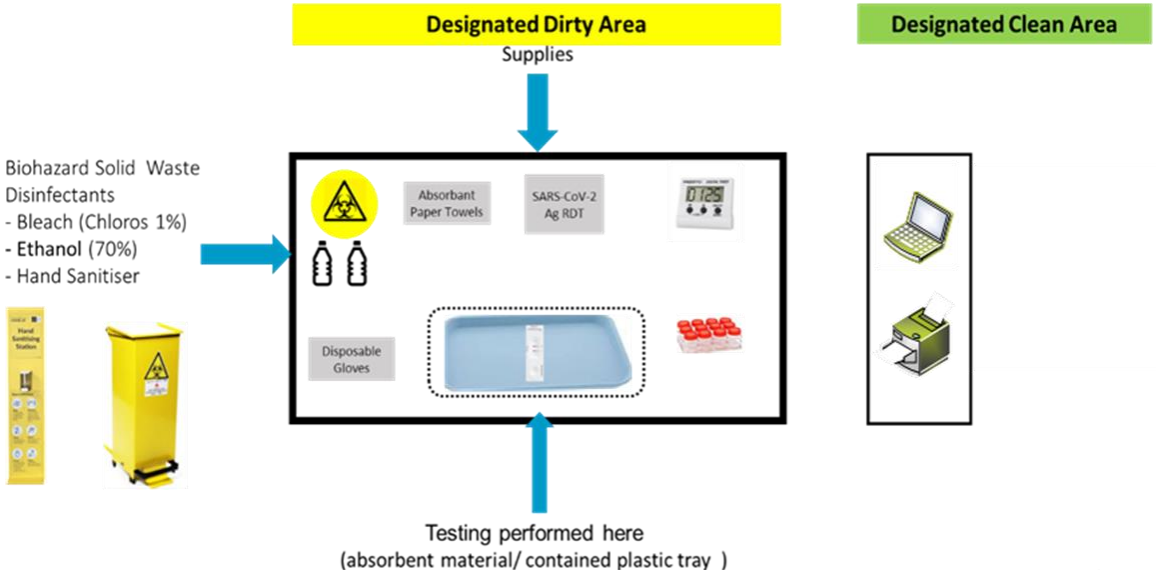
- ADT result template
- Disposable Pen

The following may be required based on the setting:

- Internet connection
- Laptop
- Printer
- Phone
- RADT result template

10.2.2 Workstation Configuration

The below diagram is an indicative setup of an ADT sampling and testing station with designated dirty and clean areas. These requirements may differ depending on the specific setting and workflows.



10.2.3 Preparation of workstation

1. Clean and disinfect the workstation before and after use and immediately after a spill occurs.
2. Contact time, dilution and shelf life of the working disinfectant solution (after dilution) are all critical for effective disinfection (follow manufacturer's instructions on effective and safe use).
3. Always leave disinfectants in contact with surfaces or spills for the recommended time, usually 10–15 minutes.
4. Prepare working solution of sodium hypochlorite (bleach) daily by diluting from the concentrated disinfectant solution, as diluted sodium hypochlorite degrades rapidly losing efficacy.
5. Mark the date of dilution on the bottle and only use on the day of preparation.

10.3 Sample Procedure

1. Ask the individual to confirm their name, date of birth and mobile phone number to ensure they are correct on the Swiftqueue label.
2. Individuals will be directed to the dedicated area where the ADT is being undertaken.
3. Explain the swabbing procedure to the individual and that two swabs will be obtained (if applicable in the setting) and secure verbal consent. Explain that the first sample will be used for the standard PCR test and the second sample will be used for the antigen test.
4. Print 3 additional Swiftqueue (or equivalent) ID labels for individuals. Labels will be used on the COVID request form, ADT vial, and ADT cassette. An ADT label will clearly identify that it is related to antigen testing.
5. Activity and progression of all individuals will be recorded using the appointment list (or other template).

   Note: step three requirement will differ if Swiftqueue is not used as part of the referral process.

10.4 Sample Collection

Requirements:

- Samples must be collected by trained individuals (refer to HSE Guideline/training for operators/ 'swabbers').
- New (unopened) individually wrapped sterile swab **(use swabs provided in the SARS-CoV-2 ADT kit unless specified otherwise in Instructions for Use).**
- Use the primary receptacle (e.g. tube with extraction buffer). Note this may need to be pre-prepared in advance of sample collection (Section 2.6 below). Refer to specific manufacturer's Instructions for Use for the kit in question.
- Antigen Testing must be performed immediately after sample collection.
- Use only the materials and reagents (e.g. extraction buffer) the manufacturer supplied with the test.
- If testing cannot be performed immediately after sample collection, follow the manufacturer's recommendations for storage.
- **Note: the ADT swab type may vary based on the manufacturer (e.g. nasopharyngeal, nasal)**

10.4.1 Pre-collection steps

1. The batch number, lot number, and manufacturer of the test kit must be recorded in the result template.
2. Pre-prepare the extraction buffer tubes as indicated in manufacturer's instructions.
3. Provide these pre-prepared tubes and swabs provided with test kits to swab taker prior to taking specimen.

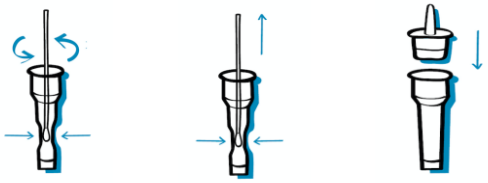
10.4.2 Sample collection

1. Confirm the individual name, date of birth and mobile phone number are correct on the Swiftqueue label (or equivalent).
2. Explain the swabbing procedure to the individual and that two swabs will be obtained (if applicable in the setting) and secure verbal consent.
3. After taking the first sample for the standard PCR test, proceed to obtaining the second sample for the ADT.
4. Apply Swiftqueue or equivalent ID label on the pre-prepared ADT vial.

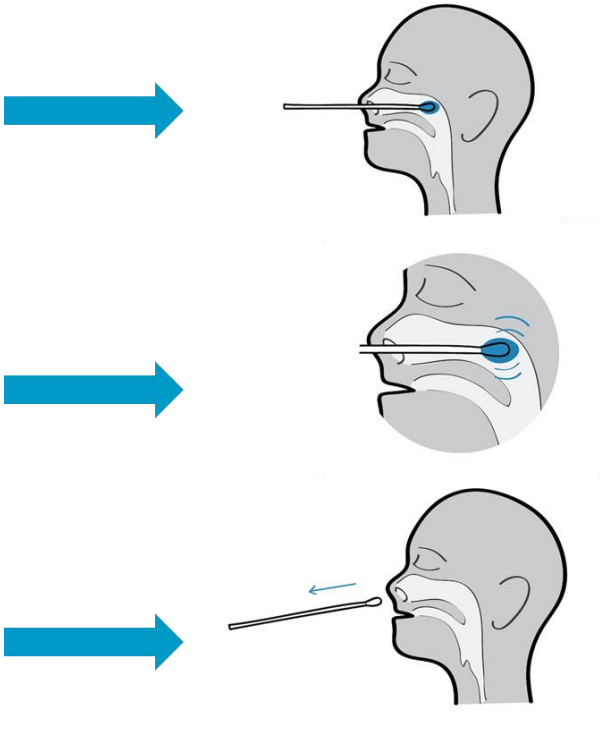
IF NASOPHARYNGEAL SWAB

5. Insert a sterile nasopharyngeal swab (provided with SARS-CoV-2 ADT kit) into the nasal cavity of the patient, reaching the surface of the posterior nasopharynx.
6. Swab over the surface of the posterior nasopharynx, rotating the swab 3−4 times to ensure a good sample. Leaving the swab in the nasal cavity for a few seconds will ensure absorption of the nasal secretions.
7. Withdraw the sterile swab from the nasal cavity.
8. Insert the swab into the labelled pre-prepared extraction buffer tube for the specified period of time.

9. While squeezing the buffer tube, rotate the swab gently. Please refer to the specific manufacturer's guidelines as there can be minor difference in the timing or number of rotations etc.
10. Remove the swab while squeezing the sides of the tube to extract the liquid from the swab. The extracted solution will be used as test sample.
11. Press the nozzle cap tightly onto the tube.
12. Pass the tube to scientist/analysts for testing as outlined below.



Refer to HSE video on obtaining nasopharyngeal swabs for further guidance.



IF NASAL SWAB

1. To avoid viscous mucus interfering with sampling, invite the individual to blow their nose before sample collection.
2. Using the sterile nasal swab, take a bilateral nasal swab from both nostrils as follows:
3. Tilt the individuals head back 70 degrees as shown below. While gently rotating the swab, insert the swab approximately 2 cm into the nostril until resistance is met at the turbinates. Rotate the swab 5 times against the nasal wall. Using the same swab repeat the collection procedure with the second nostril. Slowly remove the swab from the nostril each time.

4. Following sample collection, immediately insert the swab directly into the labelled pre-prepared extraction buffer tube provided by the scientist. The next steps can be completed immediately by the scientists/analysts, working alongside the swabber.
5. Swirl the swab tip in the buffer fluid inside the extraction tube pushing into the wall of the extraction tube at least five times and then squeeze out the swab by squeezing the extraction tube with your fingers.
6. Break the swab at the break point and close the cap of the extraction tube. The extracted solution will be used as the test sample and will be added to the kits lateral flow cassette for testing.
7. Press the nozzle cap tightly onto the tube.
8. Pass the tube to scientist/analysts for testing.

10.5 Performing the SARS-CoV-2 Antigen Diagnostic Test

Typical SARS-CoV-2 ADT kits consist of:

- Test device (individually wrapped in a foil pouch with desiccant)
- Extraction buffer tube
- Buffer
- Nozzle cap
- Paper stand for securing the extraction buffer tube
- Instructions for Use (IFU).

It is important to refer to the test-specific Instructions for Use, as reagents and procedures including incubation times may vary between different tests.

1. Check sample received against worklist form to confirm receipt of sample. This will be reconciled with ADT result template at end of day to ensure all samples were collected, tested and resulted.
2. Label the ADT vial and ADT cassette with the Swiftqueue labels (or equivalent).
3. Apply drops of extracted specimen to the specimen well of the test device. Add the exact number of drops specified by the manufacturer.
4. Read and record the test result after the specified period of time, usually 15 minutes. The exact time period specified by the manufacturer should be used.
5. Record the test result in the ADT Result template. See section below for interpretations. Ensure a checker confirms the result.
6. Dispose of all waste (used test kit, extraction buffer tube, swab and paper stand) in the

biohazard bin.

7. Remove PPE (medical mask, gown, gloves, and eye protection or face-shield) as per doffing guidelines.
8. Perform hand hygiene.

10.6 Interpreting Results

ADT results should be considered together with the patient's clinical history and other available information.

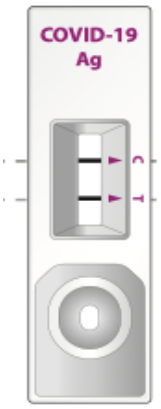
The test result MUST only be read within the recommended timeframe indicated by the Manufacturer.

It should be noted that the test procedures and interpretation of SARS-CoV-2 ADT results are similar for all tests. It is important to follow the test-specific Instructions for Use, as reagents and procedures including incubation times may vary between different tests.

Interpreting the ADT result on the cassette:

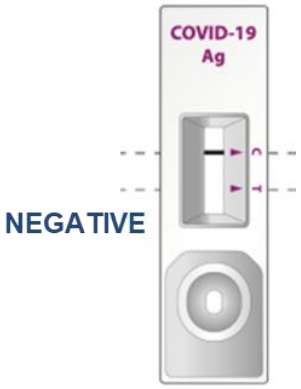
- A coloured band will appear in the top section of the result window to show that the test is working properly. This band is the control line (C).

- Depending on the ADT result, a coloured band may appear in the lower section of the result window. This band is the test line for SARS-CoV-2 antigen (T).



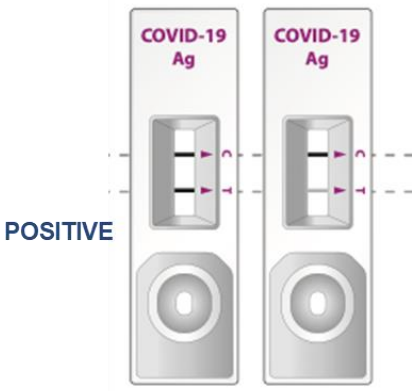
NOT DETECTED

- A line in “C” and NO LINE in “T” means SARS-CoV-2 is NOT DETECTED.
- The test result should be interpreted as a **NEGATIVE** result



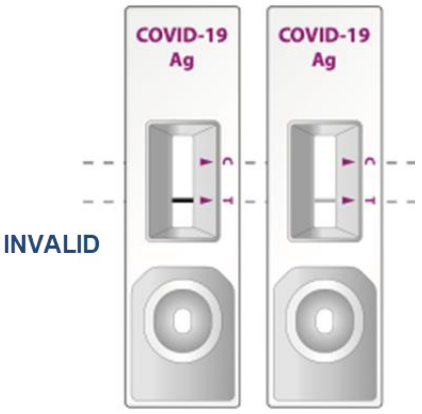
DETECTED

- A line in “C” AND a line in “T” means SARS-CoV-2 is DETECTED.
- Even if the control line is faint or the test line isn't uniform, the test should be considered to have been performed properly and the test result should be interpreted as a POSITIVE result.



INVALID

- NO LINE in “C” and a line or no line in “T” means the test is INVALID.
- Repeat the test using a new (unopened) SARS-CoV-2 ADT device and a new sample.



10.7 Managing and Recording Results

Note: a site must have a means to record results of all ADT completed. This should be captured in the ADT result template unless agreed otherwise.

This process should be performed in a separate clean area:

1. Ensure administrative individual confirms the result.
    a. **If detected,** the result must be recorded in the ADT result template. A designated member of the team must contact the individual immediately and request them to isolate. A specific script provided by contact tracing can be used to counsel and advise individuals in each of the different settings.
    b. **If not-detected,** the result must be recorded in the ADT result template.
    c. **If invalid,** the result must be recorded in the ADT result template. Either repeat the antigen test immediately using the same specimen collected or request a confirmatory PCR test if required. Clinical judgement should be applied based on the setting.

10.8 Reporting of Results

Note: reporting requirements may vary dependent on the setting. All users should refer to their settings operational plan to ensure requirements are met.

This process should be performed in a separate clean area:

1. **Where detected:**
    a. Always record each result in the ADT result template. Results must then be sent Public Health or input on the Covid Care Tracker (CCT) immediately to allow contact tracing (review operational plan for specific requirements).
    b. This positive result must also be input to the Computerised Infectious Disease Reporting System (CIDR) immediately (review operational plan for specific requirements).
2. **Where not-detected or invalid:**
    a. Results should not be uploaded to CCT currently (review operational plan for specific requirements).
    b. A summary update of all results must be sent to Public Health outlining the aggregate number of individuals who tested positive, negative, and invalid.

10.9 Activity Reporting

A summary report of ADT activity will be requested from sites to support planning and procurement. Sites are requested to provide aggregate data of activity upon request.

11.0 Quality Assurance

ADT should be conducted under the specific clinical guidance and governance as outlined in clinical governance section. A quality management system (for point of care/near-patient testing) should be implemented in line with national guidelines for safe and effective near-patient testing. Operators undertaking the sampling and testing must be documented as fully competent and trained.

This QMS should take into account the following:

- Training and ongoing competency assessment of the operator.
- Record keeping and maintenance of documentation.
- Performance and documentation of appropriate internal quality control.

- Correct patient identification.
- Obtaining a satisfactory sample and sample integrity.
- Performance of the test in accordance with the manufacturer's instruction.
- Recording of the test result in the patient record.
- Correct interpretation of the result and appropriate action taken.
- Recording of non-conformances, and corrective and preventive actions.
- Performance of quality indicators (IQC and EQA).

11.1 Batch Acceptance

All batches of SARS-CoV-2 ADTs should be checked by lot testing, i.e. by evaluating the performance of production lots (batches) before they are deployed in the field.

- New lot testing helps to ensure that the SARS-CoV-2 ADTs delivered to the sites perform according to the manufacturer's specifications.
- New lot testing is usually carried out in the laboratory, following standardized procedures and using QC materials (detected and not-detected controls).
- At least five samples (three detected and two not-detected) should be tested for each new lot.
- New lot testing can be conducted with QC materials.

11.2 Internal Quality Controls:

For SARS-CoV-2 ADTs, the controls come in the form of:

- In-built internal procedural controls that validate the test sample has travelled through the intended reaction area (often in lateral flow designs).
- IQC can also involve the use of quality control materials (some manufacturers provide these as part of the assay e.g. positive and negative swab control) that act as positive and negative controls.
- Alternatively, use third party quality control materials such as proficiency testing panels as they become available, or patients' samples already tested with results known from a verified method/assay.
- The operators performing the tests must ensure that IQC is performed correctly and consistently.
- Internal controls should be performed weekly or more frequently depending on the number of tests being performed.

11.3 External Quality Assessment:

EQA is a means of determining how a particular diagnostic test is performing in comparison to a similar diagnostic test at different sites and to other manufacturers' tests or other laboratory analysers.

To establish high quality and comparability of antigen test results for SARS-CoV-2, EQAs suitable for antigen tests should be used at regular intervals and performance should be reviewed under a quality management system.

Currently, there are two EQA schemes for SARS-CoV-2 ADTs, which are due to commence shortly:

- INSTAND EQA Scheme Virus Antigen Detection SARS-CoV-2 antigen – March 2021 (410).

- Lab quality, 5681 SARS-CoV-2, antigen detection EQA scheme.
- Proficiency testing panels may become available.

12.0 Training

A training package has been developed, adopting material and guidance from the SARS-CoV-2 ADT training package v1.0 which has been designed and developed by the Foundation for Innovative New Diagnostics (FIND) and the World Health Organization (WHO). The training package addresses the theoretical and practical components of SARS-CoV-2 ADT testing and provides operators with the skills and resources on how to safely perform SARS-CoV-2 ADT testing.

It also includes competency assessment which should be carried out after the initial training to determine whether participants have understood the content of the training, can safely and accurately perform the sample collection and testing, and can interpret and record the test result(s). The operators should be observed carrying out the entire process and should process a minimum of two SARS-CoV-2 ADTs during the training, each tester will be asked to independently perform two complete SARS-CoV-2 ADT tests in parallel.

To pass the competency assessment, trainees should obtain a passing score of 80% on the competency assessment. This must be signed off and documented.

13.0 Revision and Audit

This document will be revised and updated in line with ADT developments.

14.0 References

- HPSC: Interim guidance on use of Antigen Detection Tests in the public health system in Ireland, Version 1.0, January 2021.
- The SARS-CoV-2 Ag RDT v1.0 training package designed and developed by FIND and World Health Organization (WHO) 2020.
- Guidelines for safe and effective near-patient testing (NPT). Approved for soft release by the National Near-Patient Testing (NPT) Consultative Group, Dublin, Ireland April 20,2020.
- Infection Prevention and Control Guidance, HPSC, 2020.
- COVID-19 Awareness and Poster Material, HSE 2021.