

## GEBRUIK VAN GEAUTOMATISEERDE ANTIGEENTESTS

RAG subgroep Testing – 19 april 2021

Opmerking: De huidige aanbevelingen zijn onderhevig aan veranderingen afhankelijk van nieuwe wetenschappelijke gegevens en/of de evolutie van de epidemie.

### Samenvatting en aanbevelingen:

- Geautomatiseerde Ag-tests hebben een geringere gevoeligheid dan RT-PCR-tests en de RT-PCR-test blijft daarom de voorkeur genieten bij de indicaties waarvoor hij momenteel wordt aanbevolen .
- Een uitzondering is in ziekenhuizen waar een snel resultaat vereist is en een snelle RT-PCR-test wordt aanbevolen, maar geen snelle RT-PCR-capaciteit beschikbaar is.
- Geautomatiseerde Ag-tests hebben een betere gevoeligheid dan snelle Ag-tests en kunnen daarom een goed alternatief zijn in settingen:
  - waar snelle Ag-tests momenteel worden aanbevolen of nuttig worden geacht,
  - waar een hoge verwerkingscapaciteit vereist is,
  - waar het uitvoerbaar is, en
  - waar aan de nodige veiligheidsvoorwaarden is voldaan.
- Indien er onvoldoende RT-PCR capaciteit is, kunnen geautomatiseerde Ag-tests een valabel alternatief zijn voor de screening van niet-COVID-patiënten vóór ziekenhuisopname. Patiënten die volgens de geldende ziekenhuis richtlijnen prioritair getest dienen te worden (symptomatische patiënten en asymptomatische patiënten met potentiële risico's bij aerosol-producerende procedures of met individuele risicofactoren) moeten echter steeds met een RT-PCR getest worden.
- Bij voorkeur wordt een nasofaryngeale wisser afgenomen, tenzij de fabrikant van de test anders aangeeft.
- Enkel geautomatiseerde Ag-tests die door het FAGG zijn goedgekeurd en die voldoen aan de minimumeisen inzake gevoeligheid/specificiteit mogen gebruikt worden.

### De volgende personen hebben deelgenomen aan dit advies:

Emmanuel André (KU Leuven); Bénédicte Delaere (UCLouvain); Olivier Denis (CHU-UCL Namur); Herman Goossens (UAntwerpen); Marie Pierre Hayette (CHU-Liège); Yves Lafort (Sciensano); Barbara Legiest (ZG); Tinne Lernout (Sciensano); Pieter Libin (UHasselt); Romain Mahieu (COCOM); Elizaveta Padalko (UZGent); Olivier Vandenberg (LHUB-ULB); Ann Van den Bruel (KU Leuven); Steven Van Gucht (Sciensano); Pieter Vermeersch (KU Leuven).

## CONTEXT

There exist several laboratory-based tests detecting SARS-CoV-2 antigen. The difference of these tests compared to the rapid antigen tests is that they allow high-throughput of samples on automated machines. The advantage with regards to RT-PCR is that they can process samples in less than one hour per run, which greatly shortens the turnaround time, that they are less expensive and laborious, and that they require less training. The disadvantage is that they are, similar to rapid Ag tests, less sensitive, although that they detect most infections with a high viral load. To date, no indications for the use of these automated antigen tests have been defined, and the question was asked if there is a place for them in the current test strategy.

## DISCUSSION

- The automated Ag tests that were evaluated in Belgium (the VITROS test of Ortho Clinical Diagnostics, the DiaSorin Liaison SARS-CoV-2 antigen test, and the Lumipulse G SARSCoV-2 Ag assay) all showed a better sensitivity than rapid Ag tests and detected all infections with a high viral load. They are therefore good screening tests.
- Another advantage, compared to rapid Ag tests, is that they have a high throughput.
- Automated Ag tests are easy to perform and can be used 24h/24h.
- The challenge is the inactivation step that may require a safety cabinet (for example, if the swab is not directly inserted in a deactivation buffer immediately after collection, for instance to keep the sample on UTM for further testing), which limits their use at the point-of-care or in non-medical settings. The duration of the inactivation may vary depending on manufacturers' instruction but is usually 30 minutes minimum at room temperature.

## CONCLUSIONS AND RECOMMENDATIONS

- Automated Ag tests have a lesser sensitivity than RT-PCR tests. The RT-PCR test continues therefore to be the preferred test for indications for which it is currently recommended<sup>1</sup>.
- The only exception is in settings where a rapid result is required and a rapid RT-PCR test is recommended<sup>2</sup>, but no rapid RT-PCR capacity is available, such as in smaller hospitals.
- Automated Ag tests have a better sensitivity than rapid Ag tests and can therefore be a good alternative in settings:
  - where rapid Ag tests are currently recommended or considered useful<sup>3</sup>,
  - where a high-throughput is required,
  - where it is feasible to perform them, and
  - where the necessary safety conditions are fulfilled.

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<sup>1</sup> See: Indications for the use of RT-PCR, [Dutch version](#) of [French version](#)

<sup>2</sup> See: Advice on the use of rapid RT-PCR tests (link to be inserted)

<sup>3</sup> See: Advice on the use of rapid Ag tests, [Dutch version](#) of [French version](#)

- Regarding the screening of non-COVID patients prior to hospitalization, the RT-PCR test remains the preferred test for those patients recommended to be tested in accordance with the existing guidelines for hospitals<sup>4</sup>. In the current context of high incidence, the recommendation is to test every symptomatic person, and for asymptomatic persons to prioritize in function of the testing capacity (including the requirement that the test results be available within 24 hours). The first priority are patients with potential risks in aerosol-generating procedures and patients presenting individual risk factors, and these should always be tested with an RT-PCR. The remaining admissions are preferentially tested with an RT-PCR, but can be tested with an automated Ag test if there is insufficient RT-PCR capacity.
- The preferred sample to collect is a naso-pharyngeal swab, unless the manufacturer of the test indicates otherwise.
- As for rapid Ag tests, only automated Ag tests that have been approved by the FAGG/AFMPS and that fulfill the minimal requirements with regard to sensitivity/specificity can be used.

## BACKGROUND

### Scientific literature

Unlike for rapid Ag Tests, there are only a few publications evaluating the performance of automated Ag tests. Some of these were done in a Belgian context.

Favresse et al. evaluated four rapid Ag tests (Biotical, Abbott's Panbio, Healgen, and Roche) and one automated Ag test (the VITROS test of Ortho Clinical Diagnostics) on NPS samples from symptomatic and asymptomatic people presenting for testing in Namur (1). The automated test performed much better than the rapid tests. The sensitivity of the rapid Ag tests among 58 samples with a Ct value  $\leq 25$  was 93.1% for the Biotical and the Panbio assays, and 96.6% for the Healgen and the Roche assays, versus 100% (95%CI: 95.5-100%) for the VITROS test, up to a Ct value of 33. Specificity was 100%. The fact that the VITROS assay presented better performance compared to the rapid tests was thought to be related to an increased limit of quantification made possible by the chemiluminescent technology used.

Lefever et al. evaluated the quantitative DiaSorin Liaison SARS-CoV-2 antigen test in 414 symptomatic and asymptomatic individuals (204 RT-PCR positive and 210 RT-PCR negative) consulting their general practitioner in Louvain (2). Overall sensitivity and specificity compared to RT-PCR were 67.7% [95%CI: 60.9-73.7] and 100% [95%CI: 97.8-100], respectively. Sensitivity was 100% [95%CI: 96.3-100] for samples with a viral load  $\geq 105$  copies/mL. According to Ct value, the sensitivity was 96.4% [95%CI: 91.8-98.8] for a Ct value  $< 25$  and 100% [95%CI: 96.5-100] for a Ct value  $< 23$ .

Yin et al. evaluated four rapid Ag tests (Panbio, BD Veritor, Coris and SD Biosensor) and the Lumipulse G SARSCoV-2 Ag assay of Fujirebio among one hand, 478 recently symptomatic patients for rapid Ag tests and on the other hand 214 selected UTM samples including 136

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<sup>4</sup> See: [https://covid-19.sciensano.be/sites/default/files/Covid19/Brief\\_Teststrategie%20voor%20algemene%20en%20psychiatrische%20ziekenhuizen%20en%20voor%20de%20revalidatieziekenhuizen.pdf](https://covid-19.sciensano.be/sites/default/files/Covid19/Brief_Teststrategie%20voor%20algemene%20en%20psychiatrische%20ziekenhuizen%20en%20voor%20de%20revalidatieziekenhuizen.pdf) OR [Lettre Stratégie de test pour les hôpitaux généraux et psychiatriques et pour les hôpitaux de réadaptation.pdf \(sciensano.be\)](#)

consecutive positive samples from the routine of the clinical laboratory for the automated Ag assay (3). Overall sensitivity of the rapid Ag tests (among symptomatic cases) was 83.3% and reached 86.9% for patients with symptoms since <5 days. Sensitivity of the automated Ag test was 86.7% among 15 asymptomatic cases, and reached 87.4% for Ct<20/32.

Hirotsu et al. validated the performance of the LUMIPULSE SARS-CoV-2 Ag kit based on chemiluminescence enzyme immunoassay (CLEIA) (4). The antigen test exhibited a sensitivity of 55.2% on 58 RT-PCR positive NPS samples and a specificity of 99.6% on 255 negative samples. All 17 samples with a vial load of >2 log<sub>10</sub> copies/test were detected and 6 of 10 samples with a vial load 1-2 log<sub>10</sub> copies/test. The authors concluded that the LUMIPULSE antigen test can rapidly identify SARS-CoV-2-infected individuals with moderate to high viral loads and may be helpful for monitoring viral clearance in hospitalized patients.

Koskinen et al. validated the automated mariPOC SARS-CoV-2 test, based on optical laser technology detecting viral structure proteins (5). In comparison to the PCR testing, sensitivity and specificity of the mariPOC test were 92.3% (12/13) and 100% (198/198), respectively.

Ren et al. evaluated a saliva-based N antigen assay, using an electrochemiluminescence (ECL)-based immunoassay (6). Sensitivity was 90.2%, compared to saliva-based PCR, and 100% among samples with a Ct value <35. Specificity was 100%.

Rusanen et al. evaluated detection of SARS-CoV-2 via time-resolved Förster resonance energy transfer (TR-FRET) with donor- and acceptor labeled polyclonal anti-NP and -SP antibodies (7). The NP-based assay showed 97.4% (37/38) sensitivity and 100% (10/10) specificity in comparison with virus isolation, and 77.1% (37/48) and 99.0% (95/96) in comparison with SARS-CoV-2 RT-PCR. The assay yielded positive results for all samples with Ct values of <25.

### International guidelines

No guidance on the use of automated Ag tests specifically was identified from international agencies, such as the WHO or ECDC, or from any country.

CDC adapted its guidance on rapid antigen tests in December 2020 and removed the word 'rapid', because FDA had authorized two laboratory-based antigen tests (the VITROS test and the LumiraDx SARS-CoV-2 Ag Test) (8). The guidance for the use of automated Ag tests is therefore identical to the guidance for the use of rapid Ag tests.

The Belgian Federal Agency for Medicines and Medical Products (FAGG/AFMPS) makes no differentiation between rapid/PoC Ag tests and laboratory-based/automated Ag tests, and applies the same criteria for approval.

### Examples of use of automated Ag tests

In Germany and Japan, the fully automated LUMIPULSE Ag test (Fujirebio) is used for testing passengers at international airports. In Germany, Centogene operates test centers at several international airports in which they offer (paid) tests to arriving and departing passengers (9). Test options include a PCR test, of which the result is available within 24 hours and that costs €69, and an antigen test of which the result is available after about 30 minutes and that costs €59. In Japan, the test is done on saliva samples (10).

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