High Quality Laboratory SARS CoV-2 Antigen Testing to Support the Global Pandemic Response

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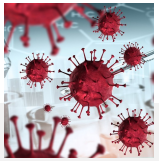
The Beckman Coulter History

CHEMISTRY

IMMUNOASSAY

URINALYSIS

HEMATOLOGY



INFECTIOUS DISEASE

1935
Dr. Beckman founded National Technical Laboratories

1949
Coulter Principle—a way to count and size microscopic particles, patented in 1953

2011
Beckman Coulter was acquired by Danaher

2018
Beckman Coulter Diagnostics launched DxH 900 hematology analyzer

2020
Launch SARS-CoV-2 Test Portfolio with High Medical Value

Danaher's Comprehensive Response to COVID-19

BECKMAN COULTER
Developed a Serology Assay to Identify IgG Antibodies to SARS-CoV-2

CEPHEID
Xpert® Xpress SARS-CoV-2 a rapid molecular diagnostic for qualitative virus detection

CHEMTREAT
Ensures customers get the water treatment solutions for essential operations

CYTIVA
Co-developing an experimental vaccine for COVID-19 with the University of Queensland

HEMOCUE
Using scrapped pallets of plastic film to make 3D printed head visors

IDT
Primer & Probe kits are a key component in CDC EUA testing protocol for diagnosis & detection of COVID-19

LEICA BIOSYSTEMS
Pathologists use Aperio AT2 DX Scanner to remotely diagnose pathology cases from home

PALL
Part of a consortium led by the University of Oxford which has a leading vaccine candidate for COVID-19

RADIOMETER
Blood Gas instruments help health care providers measure key paramaters in critically ill patients

VIDEOJET
Ensures customer production lines run smoothly so they can keep retail shelves around the world stocked with necessities – from cereal to medicines

Demand for COVID-19 Testing Rising

Vaccine distribution and therapy development are taking time and we will have to deal with COVID-19 for longer[1]

There is a rising number of COVID-19 cases around the world as we prepare for a third wave of infections[2]

Quarantine fatigue plus flu season, colder weather is propelling people to look for alternative options to deal with the pandemic[3]

1. https://www.bloomberg.com/features/2020-coronavirus-drug-vaccine-status/ [Accessed: October 19, 2020]
2. https://www.nytimes.com/live/2020/10/15/world/covid-coronavirus [Accessed: October 19, 2020]
3. https://www.vox.com/future-perfect/2020/9/28/21451436/covid-19-coronavirus-pandemic-fall-winter-third-wave [October 19, 2020]

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Demand for COVID-19 Testing Rising

World Health Organization

- The limited coverage of laboratory services and long turnaround times has meant that NAAT capacity has been insufficient to meet demand in many countries, particularly in low- and middle-income countries (LMICs)

1

SUPPLY & COST

- With a **shortage of PCR tests**, antigen testing is a suitable alternative
- Antigen tests can help labs **conserve PCR tests for patients** when the negative antigen test is inconsistent with the clinical context
- Antigen test can be a superior front line of testing defense because of **greater availability and lower pricing**

2

A MATTER OF TIME

- There may be value in providing results with antigen tests even though they may have lower sensitivity than RT-PCR tests in settings where a **rapid turnaround time is required**

(for example, these days it is taking 3-4 days to get PCR test results; while a lab antigen test result can be received in a few hours)

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1.https://www.reuters.com/article/health-coronavirus-rapid-tests/countries-turn-to-rapid-antigen-tests-to-contain-second-wave-of-covid-idUSL8N2H44VF [Accessed: October 19, 2020]
2.https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html [Accessed: October 19, 2020]

Options for the use of rapid antigen tests for COVID-19 in the EU/EEA and the UK

19 November 2020

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

- Rapid antigen tests: can contribute to overall COVID-19 testing capacity, offering advantages in terms of shorter turnaround times and reduced costs

- Test sensitivity for rapid antigen tests is generally lower than for RT-PCR

- ECDC agrees with the minimum performance requirements set by ***WHO at ≥80% sensitivity*** and ***≥97% specificity***
  <> while suggests *aiming to use tests with a performance closer to RT-PCR,* ***i.e. ≥90% sensitivity and ≥97% specificity***

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The Need for Lab Testing

- POC antigen tests are **resource intensive to scale to address high volume testing needs**[1]
- **Workflow breaks down due to many labor intensive steps in the testing process when** POC test is scaled to deliver results for 100 or 1,000 individuals
- POC tests require them to **manually record patient data into their EMR or by some other manual process**

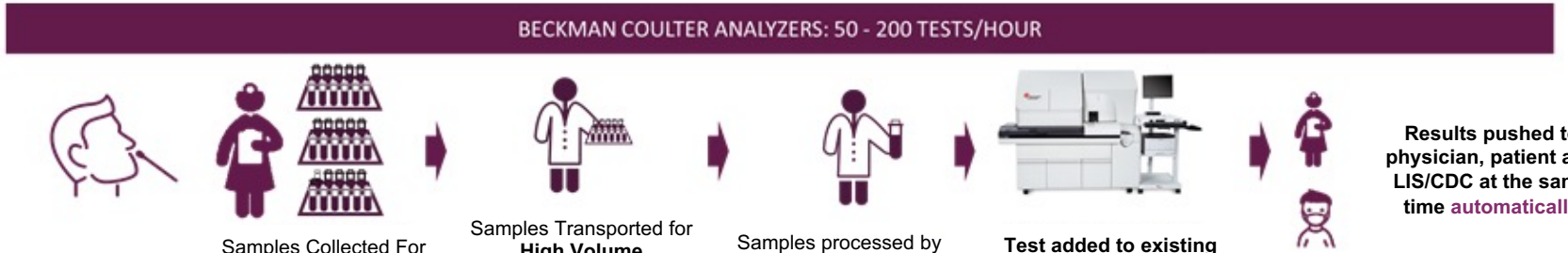
1. https://www.the-scientist.com/news-opinion/the-push-to-deploy-at-home-antigen-tests-for-covid-19-67831 [Accessed: October 12, 2020]

ACCESS SARS-CoV-2 Antigen test: *Intended Use*

- chemiluminescent immunoassay intended for the qualitative detection of ***nucleocapsid antigen*** from SARS-CoV-2 in ***nasopharyngeal*** and ***nasal swab specimens*** in transport media from individuals who are:

  - ***suspected of COVID-19*** by their healthcare provider ***within the first seven days of symptom onset*** or
  - ***for screening of individuals without symptoms*** or other reasons to suspect COVID-19 infection

Beckman Coulter's Automated High-Volume SARS-CoV-2 Antigen Testing is Low-Touch and Allows for Mass Scale Testing



Beckman Coulter Family of Immunochemistry Analyzers

ACCESS 2
IMMUNOASSAY SYSTEM

100 tests per hour

UniCel DxI 600 ACCESS
IMMUNOASSAY SYSTEM

200 tests per hour

UniCel DxI 800 ACCESS
IMMUNOASSAY SYSTEM

400 tests per hour

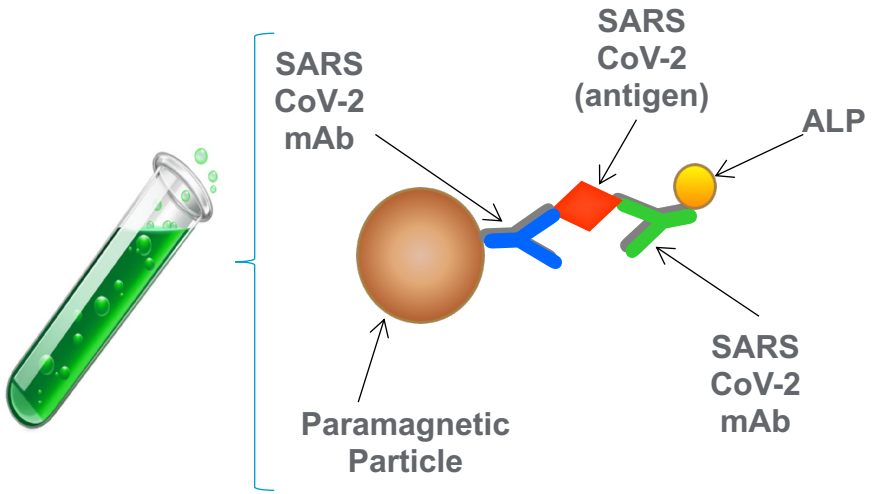
From 50 tests per hour ⟷ **200 tests per hour**

Access SARS CoV-2 Ag test:

to

ACCESS SARS-CoV-2 Antigen test:

one-step sandwich immunoassay



Paramagnetic particles coated with mouse monoclonal antibody against the SARS-CoV-2 nucleocapsid protein (*solid phase*)

+

Patient samples (extracted)

+

Mouse monoclonal antibody against the SARS-CoV-2 nucleocapsid protein alkaline phosphatase conjugate

↓

Incubation

↓

Washing

↓

+ Chemiluminescent substrate

↓

Luminometer

By comparison of the light intensity with the cut-off value determined during calibration on the instrument, the presence or absence of SARS-CoV-2 Ag is determined

	Characteristics
Test Name	ACCESS SARS-CoV-2 Antigen
Analyte Detected	Nucleocapsid antigen from SARS-CoV-2
Sample type	Nasopharyngeal or Nasal Swab
Sample stability (nasopharyngeal and nasal swab in transport media)	20-25 ºC: 24 hours 2-8 ºC: 48 hours - 20 ºC (or colder): 30 days
Open pack stability (2-8 ºC)	28 days
Calibration curve stability	28 days
Sample volume (extracted)	110 µl
Test result	Qualitative
System default unit	S/CO
Time to first result	~30 minutes
ACCESS SARS-CoV-2 Antigen calibrators	C0-C1, 2.5 mL/vial
ACCESS SARS-CoV-2 Antigen QC	6.0 mL/vial, 3 vials each level

ACCESS SARS-CoV-2 Antigen test: Results' interpretation

Result	Interpretation	Reporting Instructions
< 1.00 S/CO SARS-CoV-2 Antigen	Non-Reactive	Report result as negative for SARS-CoV-2 Antigen. The presence of SARS-CoV-2 Antigen is not detected.
≥ 1.00 S/CO SARS-CoV-2 Antigen	Reactive	Report result as positive for SARS-CoV-2 Antigen. The presence of SARS-CoV-2 Antigen is detected

CLINICAL PERFORMANCE
Nasopharyngeal Specimen

- 62 nasopharyngeal swabs in 3 mL Bartel® FlexTrans™ Transport Medium and 18 nasopharyngeal swabs in 2 mL Remel MicroTest™ M4RT®
- The samples were enrolled **from symptomatic patients** suspected of COVID-19 at two locations in France and USA and tested within 48 hours of collection or frozen
- Patients who presented **within 7 days of symptom onset** were included in the study
- An FDA Emergency Use Authorized **RT-PCR assay** for the detection of SARS-CoV-2 was utilized as the **comparator method** for this study

Access SARS-CoV-2 Antigen	Comparator Method		
	Positive	Negative	Total
Reactive	28	0	28
Non-Reactive	2	50	52
Total	30	50	80

- **Positive Percent Agreement: 28/30, 93.3% (95% CI: 78.7-98.2%)**
- **Negative Percent Agreement: 50/50, 100.0% (95% CI: 92.9-100.0%)**

CLINICAL PERFORMANCE
Nasal Specimen

- 27 nasal swabs in 3mL Copan UTM™ and 57 nasal swabs in 3mL Remel MicroTest™ M4RT®
- The samples were retrospectively enrolled from **asymptomatic patients** suspected of COVID-19 in the USA, and frozen prior to testing
- An FDA Emergency Use Authorized **RT-PCR** assay for the detection of SARS-CoV-2 was utilized as the **comparator method** for this study

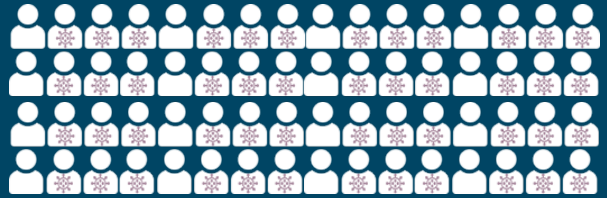
Access SARS-CoV-2 Antigen	Comparator Method		
	Positive	Negative	Total
Reactive	45	0	45
Non-Reactive	4	35	39
Total	49	35	84

- Positive Percent Agreement 45/49 - 91.8% (95% CI: 80.8 - 96.8%)
- Negative Percent Agreement 35/35 - 100.0% (95% CI: 90.1 - 100.0%)

Confidence in Antigen Test Results due to Supporting Data in all Patient Populations

Confirmatory PCR testing following a negative antigen test may not be necessary if:

- the pretest probability is low,
- the person is asymptomatic or
- has no known exposures, or
- is part of a cohort that will receive rapid antigen tests on a recurring basis



Confirmatory PCR testing following a positive antigen test may not be necessary when:

- the pretest probability is high,
- the person is symptomatic

Source: https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html [Accessed: October 19, 2020]

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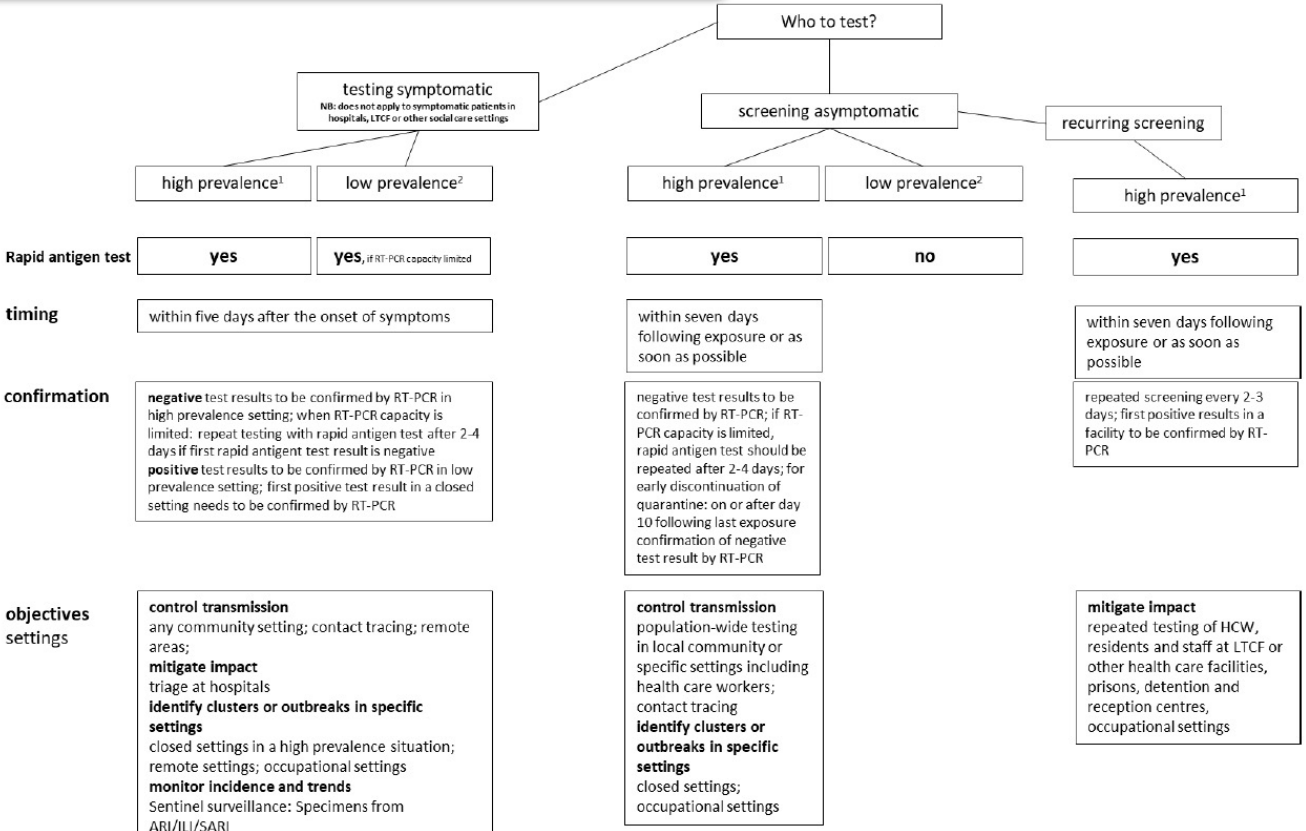
Antigen Testing for Different Purposes



[1]RT-PCR capacity is limited [2]RT-PCR capacity is likely sufficient

European Centre for Disease Prevention and Control. Options for the use of rapid antigen tests for COVID-19 in the EU/EEA and the UK. 19 November 2020. ECDC: Stockholm; 2020.

Cross reactivity and microbial interference

Potential Cross-reactant	Concentration	Cross-Reactive Result
Human coronavirus 229E	1.04×10^5 $TCID_{50}$/mL	Non-reactive
Human coronavirus OC43	1.05×10^5 $TCID_{50}$/mL	Non-reactive
Human coronavirus NL63	1.00×10^5 $TCID_{50}$/mL	Non-reactive
MERS coronavirus	1.00×10^5 $TCID_{50}$/mL	Non-reactive
Adenovirus	$1.00 \times 10^{5.14}$ U/mL	Non-reactive
Human Metapneumovirus (hMPV)	1.51×10^5 U/mL	Non-reactive
Parainfluenza virus 1	1.80×10^5 $TCID_{50}$/mL	Non-reactive
Parainfluenza virus 2	1.00×10^5 U/mL	Non-reactive
Parainfluenza virus 3	1.32×10^5 U/mL	Non-reactive
Parainfluenza virus 4a	1.00×10^5 $TCID_{50}$/mL	Non-reactive
Influenza-A H3N2	1.00×10^5 $TCID_{50}$/mL	Non-reactive
Influenza-A H1N1	1.15×10^5 U/mL	Non-reactive
Influenza B	1.00×10^5 U/mL	Non-reactive
Enterovirus	1.51×10^5 U/mL	Non-reactive
Respiratory syncytial virus	1.05×10^5 U/mL	Non-reactive
Rhinovirus	1.18×10^5 U/mL	Non-reactive
Haemophilus influenza	1.09×10^6 CFU/mL	Non-reactive
Streptococcus pneumoniae	4.16×10^6 CFU/mL	Non-reactive
Streptococcus pyogenes	3.80×10^6 CFU/mL	Non-reactive
Bordetella pertussis	1.19×10^6 CFU/mL	Non-reactive
Mycoplasma pneumoniae	3.16×10^6 CCU/mL	Non-reactive
Chlamydia pneumoniae	1.75×10^6 IFU/mL	Non-reactive
Legionella pneumophila	1.42×10^6 CFU/mL	Non-reactive
Mycobacterium tuberculosis	1.14×10^6 CFU/mL	Non-reactive
Staphylococcus aureus	1.20×10^6 CFU/mL	Non-reactive
Staphylococcus epidermidis	1.85×10^6 CFU/mL	Non-reactive
Pooled human nasal wash – representative of normal respiratory microbial flora	N/A	Non-reactive
Candida albicans	1.56×10^6 CFU/mL	Non-reactive
Pneumocystis jiroveci-S. cerevisiae Recombinant	1.02×10^6 CFU/mL	Non-reactive

- Interference was evaluated with each sample in the presence of heat inactivated SARS-CoV-2 at three times the limit of detection, at a minimum concentration of 105 TCID50/mL or U/mL for viruses and 106 CFU/mL, CCU/mL or IFU/mL for bacteria

- No cross reactivity or microbial interference was observed for any tested organism

HKU1: Homology for HKU1 and SARS-CoV-2 is relatively low, at 35.4%

SARS-CoV: Homology for SARS-CoV and SARS-CoV-2 is high as expected, at 90.5%

Endogenous interfering substances

Interfering Substance	Concentration	Cross-Reactive Result	Interference Results
Afrin (Oxymetazoline hydrochloride)	0.075 mg/mL	Non-reactive	Reactive
Whole blood	4%	Non-reactive	Reactive
Benzocaine	1.5 mg/mL	Non-reactive	Reactive
Menthol	1.5 mg/mL	Non-reactive	Reactive
Fluticasone propionate	5% v/v	Non-reactive	Reactive
Phenylephrine hydrochloride	15% v/v	Non-reactive	Reactive
Oseltamivir phosphate	5 mg/mL	Non-reactive	Reactive
Mucin protein	0.5%	Non-reactive	Reactive
Tobramycin	4 µg/mL	Non-reactive	Reactive
Naso GEL (NeilMed)	5% v/v	Non-reactive	Reactive
Cromolyn	15% v/v	Non-reactive	Reactive
Zicam	5% v/v	Non-reactive	Reactive
Homeopathic (Alkalol)	1:10 dilution	Non-reactive	Reactive
Sore Throat Phenol spray	15% v/v	Non-reactive	Reactive
Mupirocin	10 mg/mL	Non-reactive	Reactive

- **Potentially interfering substances** found in the upper respiratory tract **do not cross-react or interfere** with the detection of SARS-CoV-2 in the **Access SARS-CoV-2 Antigen assay**

Instructions For Use C69180 B February 2021

Approved Guideline - Interference Testing in Clinical Chemistry, EP07 3rd Edition. April 2018. Clinical and Laboratory Standards Institute

POC Testing is Difficult to Scale. Burden of Testing Falls on HCP.

Beckman Coulter's SARS-CoV-2 Ag*	POC Ag Tests*
• Accurate results supported with performance data in symptomatic and asymptomatic populations	• Performance data for asymptomatic populations NA
• Detects 3-97x lower quantity of virus than some POC tests (LOD=33 TCID 50/mL)	• Works best with higher viral loads- LOD at least 3x of BEC test
• High throughput - 50-200 Tests Per Hour	• Most ancillary components part of the box (swabs & tubes)
• Workflow Optimized for Mass-Screening - HCPs collect patient samples, Lab processes - Data Management and Laboratory Information Systems facilitate reporting compliance	• Low throughput: 5-20 Tests Per Hour • Workflow **Not** Optimized for Mass-Screening - Sample collection and processing at POC – less time for patient care - Some have data management - Navica app and cloud based transmission
• Lower cost/test than most POC tests in the U.S.A.	

* Based on manufacturers' labeling

** Per https://www.tractmanager.com/, Accessed January 27, 2021 and Press Releases from Abbott in 2020

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Post Infection

Access SARS-CoV-2 IgG II Assay

Access SARS-CoV-2 IgG II is a semi-quantitative assay that measures a patient's level of IgG antibodies to the spike protein of SARS CoV-2 in human serum and plasma in response to a previous SARS-CoV-2 infection providing a numerical result from 2.00-450/mL*

CE Mark labeling

*The result will be displayed as non-reactive (<10AU/mL) and reactive (>/=10AU/mL)
** At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity.

With the Access SARS-CoV-2 IgG II semi-quantitative COVID-19 antibody diagnostic tool, clinicians can:

- Establish a baseline for antibodies based on a numerical result
- Assess relative changes of an individual's immune response to the SARS-CoV-2 virus over time
- Assess whether there is a level of IgG antibodies that may be protective**

Solution »

Supporting Data & Results »

200 Tests an hour can be run on DxI 800, of the highest throughput analyzers in the market.

Also runs on DxI 600 (100 tests/hour and Access 2 (50 tests/hour)

99.9% NPA — Minimizes inaccurate results. False positive results are extremely low.

Assay characteristics:

- 2-step assay
- Results in ~30 minutes
- Results: Semi-quantitative and Qualitative
- Onboard calibration: 28 days
- Calibration: 6-point

When combined with our **IgG and IgM assays** you get a powerful **set of COVID-19 tools** to identify individuals who are actively infected or have had a previous infection

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Thank you