EurobioPlex
SARS-CoV-2 Multiplex

REAL-TIME RT-PCR

For **qualitative** real-time RT-PCR

REF **EBX-041**

96 reactions

CE IVD

Version 1.00 of 2020/03/25

Validated on:

- CFX96™ Real Time PCR detection system (Bio-Rad) with analysis on CFX Manager version 3.1 (Bio-Rad)
- LightCycler®480 Instrument II (Roche) with analysis on LightCycler® 480 software v1.5 (Roche)
- Applied Biosystems® 7500 Real-Time PCR Systems (Applied Biosystems) with analysis on 7500 Software v2

Storage conditions:

Keep all reagents between -15°C and -22°C until use and after first use

Instructions for use

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INTRODUCTION AND INTENDED USE

SARS-CoV-2/Covid-19 virus appeared in China end of 2019 in the city of Wuhan. It belongs to the *Coronaviridae* family and the sub-genera *Sarbecovirus*.
Its genome consists of 29903 ribonucleic acid bases (RNA). SARS-CoV-2 is the 7th coronavirus infecting humans to be identified, since human coronavirus (HCoV) 229E, NL63, OC43, HKU1, SARS-CoV (coronavirus responsible for severe acute respiartory syndrome) and MERS-CoV (coronavirus inducing Middle-East respiratory syndrome). Eighteen genomes have been isolated and reported, amongst which BetaCoV / Wuhan / IVDC-HB-01/2019, BetaCoV / Wuhan / IVDC-HB-04/2020, BetaCoV / Wuhan / IVDC-HB-05/2019, BetaCoV / Wuhan / WIV04 / 2019 et BetaCoV / Wuhan / IPBCAMS-WH-01/2019. These sequences of SARS-CoV-2 have similarities with the ones of betacoronaviruses found in bats. SARS-CoV-2 is genetically distinct from other human coronaviruses such as the ones related to SARS and to MERS.

Symptoms can come as a cold, fever, cough, difficulty breezing, pneumonia, to severe respiratory syndrome, which can be fatal. The level of mortality is not precise at the beginning of the epidemic, around 2 % end of January. This is much less compared to 10 % for SARS-CoV or 30% for MERS-CoV. SARS-CoV-2 is highly contagious with more than 90 000 cases worldwide beginning of March 2020.
EurobioPlex SARS-CoV-2 is a test based on real-time reverse-transcription and amplification designed for qualitative determination of absence or presence of SARS-CoV-2 in a RNA extract. This test is indicated to diagnose the occurrence of this infection in humans, or complement a proven or indeterminate diagnosis.
EurobioPlex EBX-041 was designed to detect all known SARS-CoV-2 published sequences by alignment *in silico* with sequences of other coronaviruses.
A decision algorithm based on the detection of 3 targets (RdRp Gene target 1 and RdRp target 2, identical to the ones recommended by the World Health Organization (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance: published under Real-time RT-PCR assays for the detection of SARS-CoV-2 Institut Pasteur, Paris (2 March 2020)), and N Gene) can be used to determine SARS-CoV-2 patient status (see Data analysis and interpretation and limitations). The diagnostic must always be made by a physician and using the clinical context, history and symptoms of the patient.
The kit allows testing of 94 patients in addition to the positive and negative controls.
Extracted RNA is the starting material for the EurobioPlex SARS-CoV-2 kit.
It is the user's responsibility to choose extraction methods relevant to the type of samples tested.

The EurobioPlex EBX-041 has been validated on the following specimen:

- Nasopharyngeal aspirate
- Bronchoalveolar fluid
- Sputum
- Nasal swab

PRINCIPLE OF DETECTION

The EBX-041 is a test using reverse-transcription and real-time amplification of viral RNA of SARS-CoV-2 based on amplification of 3 genes (RdRp Gene Target 1, RdRp Gene Target 2 and N Gene target 3). If at least one RdRp target is positive, a SARS-CoV-2 positive diagnostic can be called (see Data analysis and Interpretation).

The kit contains one oligomix to detect the 3 targets, as well as an encapsidated control of RNA extraction and RT-PCR inhibition. The test is performed from extracted RNA from a sample, using one RT-PCR reaction in a single distinct well/tube.

The oligomix allows amplification of 3 specific targets (RdRp Gene Target 1, RdRp Gene Target 2 and N Gene target 3). This ensures sensitivity, and specificity with regard to other coronaviruses known, such as HCoV, SARS-CoV, betacoronavirus associated to bats (BtCoV) and MERS-CoV.
The RNA extraction and RT-PCR inhibition control allows to check for variations that may occur during the RNA extraction step of biological samples and real-time PCR amplification. Thus, it ensures that a negative result may be due to a bad RNA extraction, and/or due to the presence of PCR inhibitors in too large quantities.

RNA of SARS-CoV-2 is detected with specific probes of each target, labeled respectively with FAM (target 1/RdRp gene), HEX (tardet 2/RdRp gene) and Texas red (target 3/N gene). CI-ARN is detected using a CY5 labeled probe. Probes emit a specific fluorescence following their hydrolysis during the elongation of the amplification product. The measurement of the intensity of real-time fluorescence correlates with the accumulation of amplification products.

DESCRIPTION AND CONTENT OF THE KIT

The RT-PCR real-time EurobioPlex SARS-CoV-2 kit is ready to use and contains all reagents and enzymes for the detection of this virus (Table 1).

Fluorescence is emitted and individually recorded through optical measurements during the PCR. The detection of the amplified fragment is performed by a fluorimeter using the channels shown in the Table 2.

Table 1:

Cap color	Content of the kit	96 reactions	Reconstitution
Red	Enzyme Taq polymerase	1500 µl	Ready to use
Brown	Enzyme Reverse transcriptase	24 µl	Ready to use
Transparent	Oligomix	600 µl	Ready to use
Yellow	Positive Control CP-N	160 µl	Ready to use
Blue	Water = negative control (CN-H2O)	1mL	Ready to use
White	RNA Control (CI-ARN)	1200 µl	Ready to use

Oligomix: contains the primers and probes for the 3 targets and internal control CI-ARN

Table 2:

Target	Fluorophor	Excitation	Emission
Target 1/ RdRp Gene	FAM	495 nm	515 nm
Target 2/ RdRp Gene	HEX	535 nm	555 nm
Target 3/ N Gene	Texas red	585 nm	605 nm
Control RNA (CI-ARN)	Cy5	647 nm	667 nm

Equivalent channels on different real time PCR cyclers:
- Channel **FAM** (Systems ABI, SmartCycler II, Systems Mx, CFX96™/Chromo4, T-COR8™-IVD), Channel 510 (LC 480), Channel Green (RotorGene)
- Channel **HEX** (Chromo 4/CFX96, Systèmes Mx, T-COR 8®-IVD), Canal VIC (Systèmes ABI), Canal Alexa532 (SmartCycler II), Canal 580 (LC 480), Canal Yellow (RotorGene),
- Channel **Texas Red** (Chromo 4/CFX96, Systèmes Mx, T-COR 8®-IVD), LC Red 610 (LC480), Canal Orange (RotorGene)
- Channel **Cy5** (CFX96™/Chromo4, Systems ABI, Systems Mx, T-COR8™-IVD), Channel Alexa647 (SmartCycler II), Channel 660 (LC 480), Channel Red (RotorGene)

Note: On LC480 instrument II, apply color compensation for the following channels: FAM-HEX/VIC-TexasRed-Cy5 (465-510, 533-580, 533-610, 618-660).

Required material not provided:

- ◊ Biological Hood
- ◊ Real-time PCR instrument
- ◊ Micro centrifuge
- ◊ Vortex
- ◊ Plates / tubes for real-time PCR
- ◊ Micropipettes
- ◊ DNase-free RNase-free filter tips for micropipettes
- ◊ Sterile microtubes
- ◊ Gloves (powder free)

STORAGE

All reagents must be stored between -15 and -22°C.
All reagents can be used until the expiration date indicated on the label of the kit.
Many freezing/defrosting cycles (> 3x) must be avoided, and could lead to decrease in sensitivity.

CAUTIONS AND NOTES

Read carefully instructions before starting.

- ◊ The experiment must be performed by competent staff, trained to technical and safety techniques.
- ◊ The biosafety local regulations for SARS-CoV-2 testing must be followed accurately under all circumstances, using appropriate equipment and laboratories in this regard.

- ◊ Instruments must have been properly installed, calibrated and maintained according to the manufacturer's recommendations.
- ◊ It is the user's responsibility if he/she uses other non-validated equipment, and if so, the performances are not guaranteed.
- ◊ Clinical samples are potentially infectious and must be processed under a laminar flow hood.
- ◊ The experiment must be performed according to good laboratory practices.
- ◊ Do not use this kit after expiration date, mentioned on the label.
- ◊ The kit is shipped with dry ice, and the components of the kits must arrive frozen. If one or more components are defrosted, or of the tubes have been damaged, contact Eurobio Scientific.
- ◊ Once defrosted, spin down briefly the tubes before use.
- ◊ It is recommended to define three working areas: 1) Isolation of RNA, 2) Preparation of the reaction mix and 3) Amplification / Detection of amplified products.
- ◊ It is recommended to open and manipulate the positive controls away from biological samples to tests and from other components of the kit in order to avoid cross-contamination.
- ◊ Use specific lab coat and gloves (powder free) in each working area.
- ◊ Pipettes, reagents and other materials must not cross each area.
- ◊ Specific caution is required to preserve the purity of the reagents and reaction mixtures.
- ◊ Appropriate methods of preparation/extraction of RNA to produce high quality RNA and to be followed by an RNA application should be used, particularly avoiding all sources of RNase contamination.
- ◊ Always use RNase-free DNase-free filtered tips for micropipettes.
- ◊ Do not pipette with mouth and do not eat, drink or smoke in the area.
- ◊ Avoid sprays.

SAMPLES COLLECTION, TRANSPORT AND STORAGE

- ◊ Collect samples in sterile tubes.
- ◊ It is the responsibility of the user to master its own conditions of collection, transport and storage of samples, and extraction of RNA by suitable systems to produce RNA of good quality.
- ◊ The samples should be extracted immediately or stored following the recommendations in the table below (Table 3).

Table 3:

Recommendations of maximum storage of samples before extraction	
Room temperature	2 h
+ 4°C	72 h
- 20°C (preferably - 80°C)	Long term storage

- ◊ The user can refer to the World Health Organization or High Health Authority for storing samples.
- ◊ Extracted RNAs have to be stored at -80°C.

◊ Transport of clinical samples must obey local regulations. The biosafety local regulations for SARS-CoV-2 must be followed.

PROCEDURE

I- RNA extraction

It is the user's responsibility that the extraction system used is compatible with downstream real time RT-PCR technology. For this kit, we recommend to use extraction methods of viral RNA from respiratory samples, and refer to manufacturer's instructions of the extraction kit.

In the EBX-041 kit, CI-ARN on the CY5 channel can be added before extraction or in the PCR reaction. It ensures that a negative result is not due to an extraction problem or due to the presence of high amounts of RT-PCR inhibitors.
We recommend the addition of 10 µl of CI-ARN per extraction, and 50µl for elution. If the CI-ARN is added to control the RT-PCR, CI-ARN is added to the reaction mix (1 µl per PCR reaction). See real-time RT-PCR protocol for details.

CI-ARN is available from Eurobio Scientific (Ref EurobioPlex EBX-003).

II- Real-time RT-PCR Procedure

General comments:

- The positive control, and the RNA extraction and RT-PCR inhibition control (CI-ARN) contain a very high concentration of matrix. Manipulations must be performed carefully to avoid contamination.

- To control the functioning of the PCR, and steps of extraction and real-time RT-PCR amplification, it is necessary to test the positive control, as well as the negative control (water PCR provided = CN-H2O+ CI-ARN) (see II-2/6 for real-time RT-PCR protocol for details).

II-1/ Diagram of the procedure

1 - PREPARATION OF MASTERMIX

(a) For RNA samples extracted without CI-ARN

Number of reactions	N+3
Enzyme Taq polymerase	(N+3) x 12,5 µl
Enzyme Reverse trancriptase	(N+3) x 0,2 µl
Water	(N+3) x 2,3 µl
Oligomix	(N+3) x 5 µl
CI-ARN	(N+3) x 1 µl
Total Volume Mastermix	(N+3) x 21 µl

(b) For RNA samples extracted with CI-ARN

Number of reactions	N+3
Enzyme Taq polymerase	(N+3) x 12,5 µl
Enzyme Reverse trancriptase	(N+3) x 0,2 µl
Water	(N+3) x 2,3 µl
Oligomix	(N+3) x 5 µl
Total Volume Mastermix	(N+3) x 20 µl

2 - PREPARATION OF REACTIONS

Sample
20 µl Mastermix
+
5µl RNA sample

Positive Control
20 µl Mastermix
+
5µl CP-N

Negative Control
20 µl Mastermix
+
5µl Molecular biology water (CN-H2O)

Sample
20 µl Mastermix
+
5µl RNA sample

Positive Control
20 µl Mastermix
+
5µl CP-N

Negative Control
20 µl Mastermix
+
4µl Molecular biology water (CN-H2O)
+
1 µl CI-ARN

3 – REAL TIME PCR INSTRUMENT

Program	Temperature	Duration	Cycle(s)	
Reverse Transcription	45°C	10 min	1	-
Denaturation	95°C	3 min	1	-
Amplification	95°C	15 sec	40	-
	58°C	30 sec		Acquisition de fluorescence

II-2/ Detailed Procedure

1) Homogenize the tube of Enzymes, and vortex the Oligomix, CP-N, and CI-ARN tubes before starting, and centrifuge briefly.
2) Prepare the Mastermix as below. N is the number of PCR reactions (positive and negative controls included). Plan to prepare enough reagents for at least N+3 reactions (refer to part 1-(a) or 1-(b) of the previous diagram according to the case).

Case (a): For samples extracted without CI-ARN

Number of reactions	**N+3**
Enzyme Taq polymerase	(N+3) x 12,5 µl
Enzyme Reverse trancriptase	(N+3) x 0,2 µl
Water	(N+3) x 2,3 µl
Oligomix	(N+3) x 5 µl
CI-ARN	(N+3) x 1 µl
Total Volume Mastermix	(N+3) x 21 µl**

Case (b): For samples extracted with CI-ARN

Number of reactions	**N+3**
Enzyme Taq polymerase	(N+3) x 12,5 µl
Enzyme Reverse trancriptase	(N+3) x 0,2 µl
Water	(N+3) x 2,3 µl
Oligomix	(N+3) x 5 µl
Total Volume Mastermix	(N+3) x 20 µl

*** The volume difference between case (a) or (b) has no effect on performance.*

3) Homogenize the Mastermix prepared in 2) and centrifuge briefly.
4) Distribute 20 µL of Mastermix with a micropipette and filtered tips in each tube or well of a microplate for real-time PCR.
5) Add 5 µL of extracted RNA sample.
6) In parallel test the following controls:

- Positive control:
  - 20 µl Mastermix + 5 µl CP-N.
- Negative Control:
  - Case (a): For samples extracted without CI-ARN
    - 20 µl de Mastermix + 5 µl provided water (CN-H2O)
  - Case (b): For samples extracted with CI-ARN
    - 20 µl de Mastermix + 4 µl provided water (CN-H2O) + 1 µl CI-ARN

7) Close immediately the tubes, or plate with an adhesive film to avoid all contamination.
8) Centrifuge briefly to collect all the reaction mix at the bottom of the tubes or plate.
9) Program the real-time PCR instrument as follows

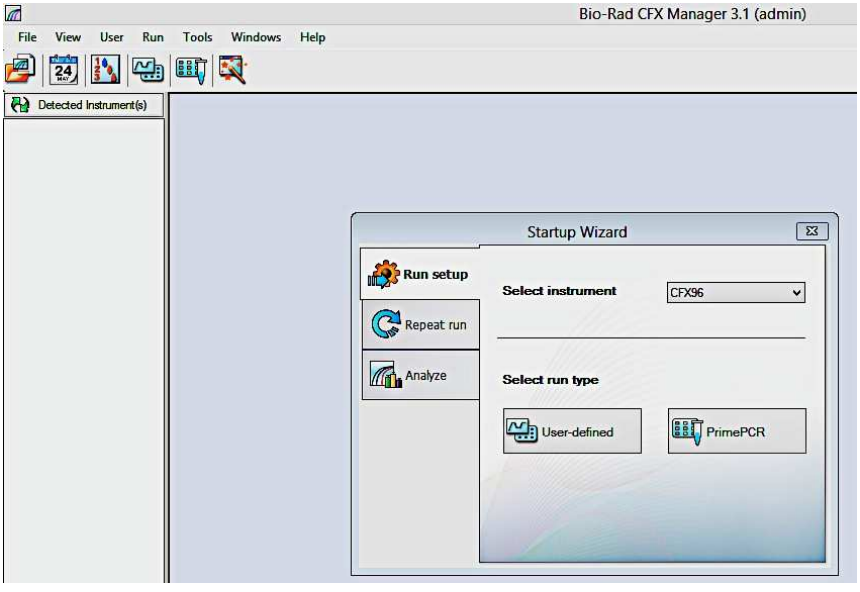
Program	Temperature	Duration	Cycle(s)	
Reverse Transcription	45°C	10 min	1	-
Denaturation	95°C	3 min	1	-
Amplification	95°C	15 sec	40	-
	58°C	30 sec		Acquisition de fluorescence

Note 1: For the Applied Biosystems systems, select “NONE” in "PASSIVE REFERENCE".
Note 2: On Rotorgene ™, please calibrate the signal by clicking on “GAIN optimization”.
Note 3: On CFX96™ (Bio-Rad), start the run using the v1.6 or later version of CFX Manager software, and analyze with v 3.1 (see § Validation of the Experiment)
Note 4: On LightCycler® 480 systems (Roche), two optical systems are available: only "System II" is compliant with use of the kit.
Note 5: On LC480 instrument II, apply color compensation for the following channels: FAM-HEX/VIC-TexasRed-Cy5 (465-510, 533-580, 533-610, 618-660).

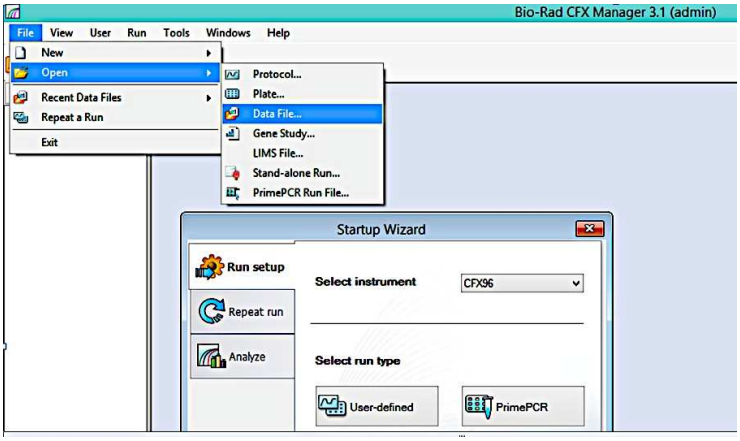
VALIDATION OF THE EXPERIMENT

The analysis of data post-acquisition on a CFX96™ PCR instrument (Bio-Rad) must be done with version 3.1 of CFX Manager software (Bio-Rad). In order to use this v3.1 version from a run started with an older version, follow the procedure below: at the end of the run, the data file with “pcrd” suffix must be open and treated with version 3.1 of CFX Manager (Bio-Rad).

If the run was done with CFX Manager v1.6 for instance, to open the data file with CFX Manager v3.1, click on CFX Manager v3.1 icon. The screen below appears.

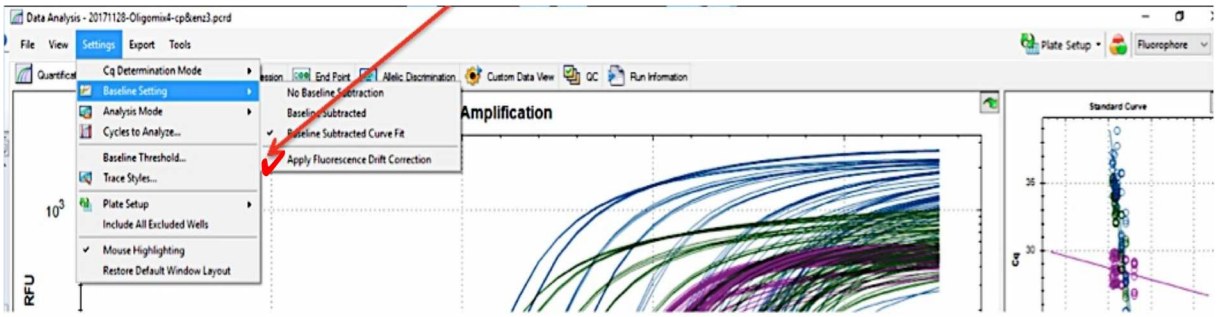


- Click on “File” and select “Open”, then “Data File”



- Select the file you want to analyze and click on “Open”.

The “drift correction” option must be selected from the “Settings” Tab, as indicated on the image below: click on “Settings”, then “Baseline Setting” then on “Apply Fluorescence Drift Correction”.



Once this is done, the analysis can start.
The results for the controls must be the following (Table 4).

Table 4: Validation of the run

Positive Control	
Texas Red	Ct ≤ 30
Negative Control	
FAM	Undetermined Ct
HEX	Undetermined Ct
Texas Red	Undetermined Ct
Cy5	Ct ≤ 40

DATA ANALYSIS AND INTERPRETATION

<u>RNA extraction and RT-PCR inhibition control in samples</u>:

The proper functioning of RT-PCR reaction can be evaluated on the Cy5 channel measuring the RNA extraction and RT-PCR inhibition control (CI-ARN) amplification.

In some cases, it is recommended to repeat the extraction or to dilute the sample 5 times, because the result cannot be interpreted (NI) (See column « validity of the test » on Table 5. All cases that can be encountered are described in Table 5.

For high viral loads detected on the FAM channel, the Ct value of CI-ARN can be increased compared to the one in the negative control. This does not invalidate positivity.

For clinical samples, and determination of presence or absence of SARS-CoV-2:

The following results are possible:

Cut-off Ct values for positivity on CFX96™, ABI® 7500, LC480®:
Target 1 and Target 2 RdRp Gene and Target 3 N gene: Ct < 40

Table 5:

Target 1 RdRp	Target 2 RdRp	Target 3 N	CI-ARN	Validity of the test	**Presence of SARS-CoV-2 or no possible interpretation (NI)**
FAM	HEX	Texas Red	CY5		
+	+/-	+/-	+ / -	Yes	**YES**
+/-	+	+/-	+ / -	Yes	**YES**
-	-	-	+	Yes	NO
-	-	+	+	Yes	Undetermined
-	-	+/-	-	*Limited*	*NI*

NI : no possible interpretation because of RT-PCR inhibition or failed extraction: no conclusion can be given. **It is then recommended to proceed to a new sampling and/or repeat the extraction and/or to dilute 5 times the sample.**

Limitations of use and interpretation:

- ❖ All samples must be treated as potentially infected by SARS-CoV-2, and biosafety local regulations must be thoroughly followed.
- ❖ Interpretation of results must take into account the possibility of false negatives and false positives.

False negative can be due to:

- Inappropriate collection of samples, or bad storage
- Samples outside the viremic phase
- Incorrect extraction methods or use of non-validated PCR instruments
- Manipulations that do not rigorously follow all the indications of this manual.

False positive can be due to:

- A contamination related to wrong manipulation of highly positive samples, or from the positive control, or PCR products

- Procedures that do not rigorously follow precautions to avoid contamination described in this manual

- ❖ Results must be interpreted by medical professionals in the clinical context of the patient, its history and symptoms.
- ❖ This test does not exclude the presence of other pathogens than the SARS-CoV-2.
- ❖ A negative result for this test does not absolutely exclude a possible infection with SARS-CoV-2.

PERFORMANCE ANALYSIS

- **Limit of detection / Analytical sensitivity:**

  - **Positive control:** 100 copies/µl CP-N.
  - **A synthetic RNA comprising the 2 genes RdRp, and N** of known concentration (10^e4 copies/ µl) spiked into a negative sample at dilution 1/10 (10 microl spiking, extraction using QIAamp viral RNA mini kit, and elution into 60 microliters) was detected.
    Sensitivity was < 16,6 copies RNA/ µl for each of the 3 targets.

- **Reproductibilité**

  Ct variability between 3 EBX-041 lots :

Coefficient of variation %	RdRp Gene Target 1	RdRp Gene Target 2	N Gene Target 3
CFX96	0,77	1,04	1,59
ABI7500	1,16	1,63	3,31
LC480	2,24	2,54	2,38

- **Diagnostics Specificity: (see also Limitations of use and interpretation)**

  This validation was carried out on:

  - 58 negative samples for known coronaviruses, some of which are positive for other respiratory viruses, in order to evaluate potential cross-reactions.
  - 13 samples positive other coronavirus than SARS-CoV-2 : CoV NL63 (n=7), CoV OC43 (n=6)

RNA extraction was performed on the following systems:
QIAamp viral RNA mini kit (Qiagen)
Magna Pure Compact (Roche Life Science)
EZ1 (Qiagen)

Number of cases	Extraction	Positive for	Coronavirus	SARS-CoV-2 status with EBX-041
2	Magna Pure compact	Adenovirus	Negative	Negative
2	Magna Pure compact	RSV A ou B	Negative	Negative
4	EZ1 or Qiagen	Influenzae A	Negative	Negative
3	Qiagen	Influenzae B	Negative	Negative
17	Qiagen	Parainfluenzae	Negative	16 Negative and 1 positive
2	Magna Pure compact	Rhinovirus	Negative	Negative
3	Magna Pure or Qiagen	Metapneumovirus	Negative	Negative
1	Magna Pure compact	Bocavirus	Negative	Negative
2	Magna Pure compact	Legionella	Negative	Negative
4	Magna Pure compact or Qiagen	Mycoplasma pneumoniae	Negative	Negative
4	Qiagen	Bordetella pertussis	Negative	Negative
2	Qiagen	Bordetella	Negative	Negative
1	Qiagen	Bordetella holmesii	Negative	Negative
1	Qiagen	Parechovirus Type 1	Negative	Negative
1	Qiagen	Parechovirus Type 2	Negative	Negative
1	Qiagen	Parechovirus Type 3	Negative	Negative
1	Qiagen	Parechovirus Type 4	Negative	Negative
1	Qiagen	Parechovirus Type 5	Negative	Negative
1	Qiagen	Parechovirus Type 6	Negative	Negative
5	Qiagen	Enterovirus	Negative	4 Negative and 1 undetermined
7	Qiagen	CoV NL63	Positive	Negative
6	Qiagen	CoV OC43	Positive	Negative

- **Diagnostic sensitivity: (see Limitations of use and interpretation)**

Evaluation was carried out on:

- 82 nasal swab samples from patients confirmed positive by a hospital using either :

  - For 65 : a « in-house » method based on the amplification of the 2 sequences on RdRp gene, recommended by WHO (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance: published under Real-time RT-PCR assays for the detection of SARS-CoV-2 Institut Pasteur, Paris (2 March 2020),

  - For 19 : Allplex 2019 n-CoV kit (Seegene).

  2 samples were evaluated with both methods.

Extraction was done using EasyMag (Biomérieux).

Resuls are the following :

		EBX-041		
		POS	NEG	TOTAL
Pre-test "in house" Method	POS	65	0	65
Pre-test Allplex 2019 n-CoV	POS	19	0	19

- 34 negative samples of nasopharyngeal aspirate, broncho-alveolar fluid, sputum, nasal swab, were supplemented with the RNA from a positive patient diluted 20-folds, from which 10 µl added to 140µl sample. Extraction was then performed on QIAamp viral RNA mini kit and eluted with 60 µl, from which 5 µl were tested with EBX-041.

All 34 samples supplemented with RNA were positive for SARS-CoV-2 with Ct as below.

	RdRp Gene Target 1	RdRp Gene Target 2	N Gene Target 3
Mean Ct +/- Standard Deviation	27.37+/-1.06	26.11+/-1.06	33.15+/-1.11
Coefficient of variation (n=34) %	3.9	4.0	3.4

Overall performances are:

		EBX-041	
		SARS-CoV-2 POS	SARS-CoV-2 NEG
Pre-test	SARS-CoV-2 POS	**116**	**0**
	SARS-CoV-2 NEG	**1**	**69**

Sensitivity : > 99 % (116/116)
Specificity : 98,6 % (69/70)
Concordance : 99,5 % (185/186)

Tests were performed on CFX96™ (Bio-rad).

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Cryopréservation de tissus, cellules et liquides biologiques issus du soin, Recommandations de bonnes pratiques, www.has-santé.fr.

WASTE DISPOSAL

Be in accordance with the law on the elimination of waste of clinical infectious material.

SYMBOLS

REF	Reference
LOT	Batch number
	Limits of storage temperature
	Expiration Date
	Content sufficient for « N » reactions
	Keep protected from light
	Manufacturer
CE	CE labeled product
IVD	In vitro Diagnostic
	Instructions for use

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