Primerdesign™ Ltd

Coronavirus COVID-19 genesig® Real-Time PCR assay

CE IVD

Instructions for Use (IFU)

Issue 4.01

GENESIG

Kits by Primerdesign

genesig®

Coronavirus COVID-19

Real-Time PCR Assay

In vitro Real-Time PCR diagnostic test for Coronavirus COVID-19

For Use with:

Sample Types	Extraction Platforms	PCR Platform
Nasopharyngeal Swabs	CE IVD Extraction System, suitable for the directed sample types QIAamp® Viral RNA Mini kit (Qiagen extraction system) exsig™ Mag extraction kit	Applied Biosystem® 7500 Bio-Rad CFX Connect™ Roche® LightCycler 480 II FluoroCycler®XT (Bruker Hain Lifescience) QuantStudio 5 (Thermofisher Scientific)
Oropharyngeal Swabs		
Sputum		
Saliva		

96 tests

IVD

REF Z-Path-COVID-19-CE

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1. Intended Use

The genesig® Real Time PCR Coronavirus COVID-19 is a CE marked, *in vitro* diagnostic real-time reverse transcriptase PCR (RT-PCR) assay intended for the qualitative detection of nucleic acid from SARS-CoV-2 in nasopharyngeal swabs, oropharyngeal swabs, saliva and sputum specimens. The assay provides rapid screening of individuals suspected of SARS-CoV-2 infection and aids the diagnosis of suspected COVID-19 disease in patients. The assay is intended for use with the extraction systems and the designated PCR platforms listed in **Sections 7 and 8**.

SARS-CoV-2 is generally detectable in specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA. Positive results do not rule out co-infection with other bacteria or other viruses. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Positive and Negative results must be combined with clinical observations, patient history, and epidemiological information.

The genesig® Real Time PCR Coronavirus COVID-19 (CE IVD) assay is intended for use by qualified and trained clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and *in vitro* diagnostic procedures.

Specimen test results are available to interpret in under three hours using the genesig® Real Time PCR Coronavirus COVID-19 (CE IVD) assay. This time includes the time to extract nucleic acid from a specimen, PCR set-up, PCR run time, and to availability of results.

2. Summary and Explanation

An outbreak of pneumonia of unknown etiology in Wuhan City, Hubei Province, China was initially reported to the World Health Organisation (WHO) in December 2019. Chinese authorities identified a novel coronavirus SARS-CoV-2 (previously called 2019-nCoV) which has resulted in confirmed human infections worldwide and cases of COVID-19 disease. Symptoms of COVID-19 disease include severe respiratory illness and has resulted in the death of patients. Patients can become infected with SARS-CoV-2 virus by person-person contact (through contact with a contaminated environment or person).

The genesig® Real Time PCR COVID-19 (CE IVD) assay is a molecular *in vitro* diagnostic test for the detection of the SARS-CoV-2 RNA in nasopharyngeal swabs, oropharyngeal swabs, saliva and sputum specimens. The assay is based on widely used nucleic acid amplification technology. The product contains oligonucleotide primers and dual-labeled hydrolysis probes, as well as control material, for the use in Real-Time RT-PCR for the *in vitro* qualitative detection of SARS-CoV-2 RNA.

Authorisations granted:

The CE marked version, genesig® Real Time PCR Coronavirus COVID-19 (CE IVD) assay (Catalogue: Z-Path-COVID-19-CE) is registered with the Medicines and Healthcare products Regulatory Agency (MHRA) and was listed as eligible for World Health Organisation (WHO) Emergency Use Listing (EUL) procurement on 7th April 2020.

The US version of the genesig® Real Time PCR COVID-19 assay (catalogue: Z-COVID-19 (US ONLY)) has been granted Emergency Use Authorization Only by the United States Food and Drug Administration (FDA) on 17th March 2020.

3. Principles of the Procedure

RNA is isolated and purified from nasopharyngeal swabs, oropharyngeal swabs, saliva or sputum using a CE IVD nucleic acid extraction system. Using polymerase chain reaction (PCR) technology the RNA is reverse transcribed to cDNA and subsequently amplified using forward and reverse primers. A fluorescent labelled probe is used to detect the amplicon. The probe system is based on the standard hydrolysis probe system known as TaqMan® Technology and the probes are labelled with fluorescent reporter and quencher dyes.

During PCR cycling, the probe anneals to a specific target sequence located between the forward and reverse primers. The probe is cleaved by the 5' nuclease activity of the Taq polymerase during the extension phase of the PCR cycle, causing the reporter dye to separate from the quencher dye, generating a fluorescent signal. With each PCR cycle, additional reporter dye molecules are released from the probe, increasing the fluorescence intensity. Fluorescence intensity is recorded at each cycle of the PCR by the Real-Time PCR machine.

The genesig® COVID-19 (CE IVD) assay includes a primers and probe mix which contains a SARS-CoV-2 specific probe labelled with the FAM fluorophore. The primer/probe mix also includes primers and probes to amplify and detect the internal extraction control RNA template supplied (genesig® Easy RNA Internal Extraction control (IEC)). The IEC specific probe is labelled with the HEX fluorophore.

The genesig® Easy RNA Internal Extraction control template is added to the nucleic acid extraction system (not provided) to provide an RNA template control, detect PCR inhibition and confirm the integrity of the PCR run. The genesig® Easy RNA Internal Extraction control template is not related to the SARS-CoV-2 viral sequence.

The oligonucleotide primers and probe for the detection of SARS-CoV-2 were selected from the orf1 ab genome region. The supplied primer/probe mix is designed for the specific detection of SARS-CoV-2 RNA (probe labelled with FAM fluorophore) and the supplied genesig® Easy RNA Internal Extraction control (IEC specific probe is labelled with HEX fluorophore).

PCR amplification has been validated using the following Real-Time PCR instruments: Applied Biosystems® 7500 Real-Time PCR System (software version 2.3), Roche® LightCycler 480 II (software version 1.5.1.62 SP3), Bio-Rad CFX Connect™ Real-time PCR Detection System (software 1.1), FluoroCycler® XT (FC XT 101, Bruker Hain Lifescience) and QuantStudio 5 (ThermoFisher Scientific, software v 1.4.3).

4. Materials Provided

The genesig® Real-Time PCR COVID-19 (CE IVD) assay contains:

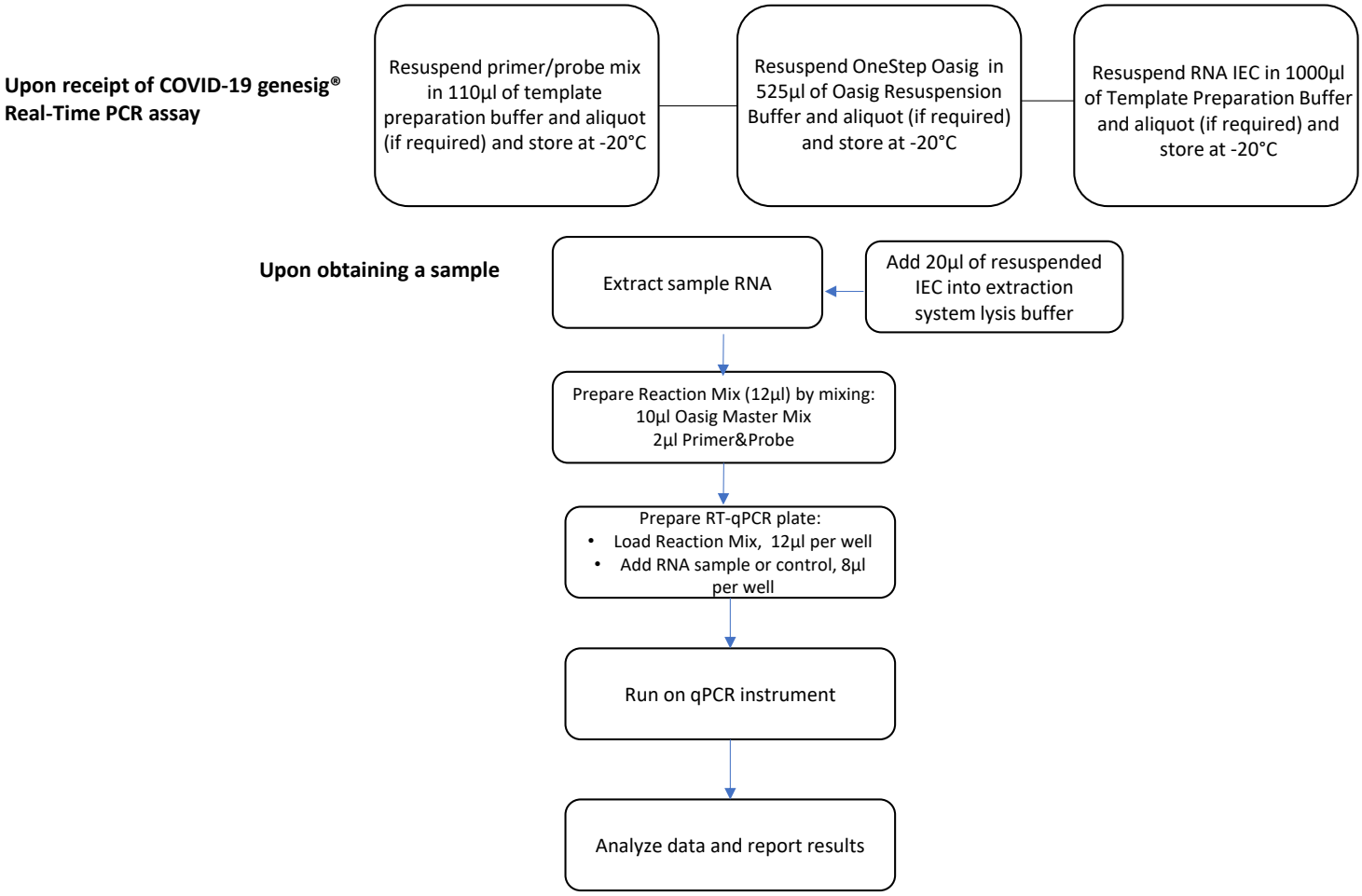
Reagent label	Number of Vials 96 tests	Volume (µL per vial)	Lid colour	Resuspended with?
Oasig™ OneStep 2X RT-qPCR Master Mix Lyophilised	2	525*	Red	Oasig™ resuspension buffer
COVID-19 Primer & Probe Mix (including IEC primer/probe mix)	2	110*	Amber	Template preparation buffer
Oasig™ resuspension buffer	2	750	Blue	n/a
Template preparation buffer	2	1500	Yellow	
Water RNase/DNase Free	1	1500	White	
genesig® COVID-19 Positive control template	1	600*	Red, vial stored in sealed foil pouch	Template preparation buffer
genesig® Easy RNA Internal extraction control (IEC)	2	1000*	Blue, vial stored in sealed foil pouch	

*The projected volume once resuspended

The COVID-19 Primer & Probe Mix contains the primers and FAM labeled probe specific to SARS-CoV-2, and includes the primers and HEX labeled probe specific to the genesig® Easy RNA Internal extraction control (IEC).

The Oasig™ OneStep 2X RT-qPCR Master Mix, COVID-19 Primers & Probes Mix, genesig® COVID-19 Positive control template and genesig® Easy RNA Internal extraction control (IEC) are all provided lyophilized. The table above indicates which buffer to use, as well as the volume to add, to resuspend these reagents.

5. Summary of Preparation and Testing Process



6. Required Equipment and Consumables (Not Provided)

- PCR hood
- Benchtop microcentrifuge
- Vortex mixer
- Adjustable micropipettes (2 or 10 µl, 200 µl and 1000 µl)
- Aerosol barrier pipette tips with filters
- Disposable gloves
- 10% bleach (1:10 dilution of commercial 5.25-6.0% hypochlorite bleach)
- DNA/RNA remover
- qPCR reaction plates compatible with the Real time PCR instrument to be used
- Water RNase/DNase free
- Plate seal

7. Real-Time PCR instruments

The genesig® Real-Time PCR COVID-19 (CE IVD) assay has been validated with the following Real-Time PCR instruments:

- Applied Biosystems® 7500 Real-Time PCR System (software version 2.3, catalogue no: 4351104)
- Roche® LightCycler 480 II (software version 1.5.1.62 SP3, catalogue no: 05015278001)
- Bio-Rad CFX Connect™ Real-Time PCR Detection System (Maestro™ software version 1.1, catalogue no: 1855201,1855195)
- FluoroCycler® XT (FC XT 101, Bruker Hain Lifescience)
- QuantStudio 5 (ThermoFisher Scientific, QuantStudio Design & Analysis Software v 1.4.3)

N.B. *please ensure that all instruments used have been installed, calibrated, and maintained according to the manufacturer's instruction and recommendations.*

8. Extraction Kits / Instruments

The genesig® Real-Time PCR COVID-19 (CE IVD) assay has been validated using the following extraction systems:

- Automated extraction system GenoXtract® from HAIN Lifescience GmbH (Brucker) using GXT NA Extraction kit (Catalogue no: 12.08.02)
- Qiagen extraction system with QIAamp® Viral RNA Mini kit (Catalogue no: 163013348, Qiagen, Germany)
- exsig™ Mag extraction kit from Primerdesign Ltd. (Catalogue no: Z-exsig™ Mag)

Please consult the IFU of the chosen extraction system for full usage details.

9. Facilities/Training Requirements

Testing for the presence of SARS-CoV-2 RNA should be performed in an appropriately equipped laboratory by staff trained to the relevant technical and safety procedures:

Refer to the UK Government guidance on handling and processing potential COVID-19 samples in laboratories:
www.gov.uk/government/publications/wuhan-novel-coronavirus-guidance-for-clinical-diagnostic-laboratories/wuhan-novel-coronavirus-handling-and-processing-of-laboratory-specimens

Refer to the World Health Organization Interim guidance on laboratory biosafety: www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance
from 13 May 2020.

And the Centers for Disease Control and Prevention (CDC) guidelines:
Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with SARS-CoV-2: https://www.cdc.gov/coronavirus/2019-nCoV/lab-biosafety-guidelines.html

10. Warnings and Precautions

10.1 General

- For in vitro diagnostic use (IVD) only.
- Handle all specimens as if infectious using safe laboratory procedures. Specimen processing should be performed in accordance with national biological safety regulations.
- Perform all manipulations of potential live virus samples within a class II (or higher) biological safety cabinet (refer to the guidance detailed in **Section 9**).
- Follow necessary precautions when handling specimens. Use personal protective equipment (PPE) consistent with current guidelines for the handling of potentially infectious samples.
- Use personal protective equipment such as (but not limited) gloves, eye protection and lab coats when handling kit reagents while performing this assay and handling materials including samples, reagents, pipettes and other equipment and reagents.
- Please consult the safety data sheet (SDS) before using this kit, which is available on request.
    - The genesig® Real-Time PCR COVID-19 (CE IVD) assay component “Template preparation buffer” contains EGTA. This component should be handled according to the SDS. In the event of damage to protective packaging, contact Primerdesign for instructions.

10.2 Preventing Contamination

- Amplification technologies such as PCR are sensitive to accidental introduction of PCR product from previous amplifications reactions. Incorrect results could occur if either the clinical specimen or the real-time reagents used in the amplification step become contaminated by accidental introduction of amplification product (amplicon).
- The genesig® COVID-19 positive control template is provided in a sealed foil envelope and contains a high copy number of templates. It should be opened and processed away from test samples and kit components to avoid cross-contamination.
    - Maintain separate areas for handling of specimen preparation, pre-PCR assay setup, and post-PCR amplified nucleic acids.
    - Maintain separated, dedicated equipment (e.g. pipettes, microcentrifuge) and supplies (e.g. microcentrifuge tubes, pipette tips) for handling of specimen preparation, pre-PCR assay setup, and post-PCR amplified nucleic acids.
    - Wear a clean lab coat and disposable gloves when setting up assays.
    - Change gloves regularly and whenever contamination is suspected.
    - Keep reagent and reaction tubes capped or covered as much as possible.
    - Always check the expiration date prior to use. Do not use expired reagent. Do not substitute or mix reagent from different kit lots or from other manufacturers.
    - Change aerosol barrier pipette tips between all manual liquid transfers.
    - During preparation of samples, compliance with good laboratory techniques is essential to minimize the risk of cross-contamination between samples and the inadvertent introduction of nucleases into samples during and after the extraction procedure. Good aseptic technique should always be used when working with nucleic acids.
    - When mixing reagents by pipetting up and down, this should be done with a volume roughly equal to 50% of the total component volume.
    - **DO NOT** use water to resuspend the kit components. Use the appropriate buffers (provided with the kit) as instructed in the table in **Section 4**.
    - Work surfaces, pipettes and centrifuges should be cleaned and decontaminated with cleaning products (e.g.10% bleach, ethanol, DNA/RNA remover) to minimize risk of nucleic acid contamination.
- RNA samples should be maintained on a cold block or on ice during preparation and used to ensure stability.
- After each run has been set up and performed, clean work surfaces and equipment with a DNA/RNA remover.
- Handle post-amplification plates with care to ensure that the seal is not broken.
- Dispose of unused kit reagents and human specimens according to national regulations (refer to guidance detailed in **Section 9**).

10.3 Prevent DNase/RNase contamination

- Use DNase/RNase free disposable plasticware and pipettes reserved for DNA/RNA work to prevent cross-contamination with DNases/RNases from shared equipment.
- Use DNase/RNase free filter tips throughout procedure to prevent aerosol and liquid contamination.

10.4 Specimen nucleic acid extraction kit/system

- Please consult the relevant Instruction For Use (IFU) and Safety Data Sheet (SDS), available from the manufacturer, before using your chosen extraction kit/ system.

11. Reagent Storage, Handling and Stability Conditions

11.1 Storage conditions

- The genesig® Real-Time PCR COVID-19 (CE IVD) assay is shipped at ambient temperatures but must be stored at -20°C upon arrival.
- The genesig® Real-Time PCR COVID-19 (CE IVD) assay should be stored in the original packaging and is stable for up 18 months once stored at -20°C.
- Repeated thawing and freezing should be kept to a minimum and should not exceed 5 freeze-thaw cycles.
- If the kit's protective packaging is damaged upon receipt, please contact Primerdesign for instructions. Attention should be paid to the "use by" date specified on the pack label and individual tube labels. On this date, the kit should be discarded following the disposal instructions in **Section 19.**
- Always check the expiration date prior to use. Do not use expired reagents.
- Primer/probe mix, the enzyme master mix, positive control template and RNA internal extraction control are all delivered lyophilized and must be resuspended in the appropriate supplied buffer to the correct volume as detailed in the table in **Section 4.**
- Once resuspended, components may be aliquoted into smaller volumes, if required, and are stable for up to six months if stored at -20°C.
- It is important to protect the fluorogenic primer/probe mix from light as this reagent is photosensitive.

11.2 In Use Stability

- The genesig® Real-Time PCR COVID-19 assay should be stored in the original packaging and is stable for up to six months once resuspended and stored at -20°C.
- The kit should not be used past the "use by" date as indicated on the pack label and individual tube labels.
- When *in use* the kit components should be returned to the freezer promptly after use to minimize the time at room temperature.
- Repeated thawing and freezing should be kept to a minimum and should not exceed 5 freeze-thaw cycles. Components may be aliquoted into smaller volumes after resuspension, if required.

12. Specimen Collection, Handling and Storage

12.1 Collecting the Specimen

Inadequate or inappropriate specimen collection, storage and transport are likely to yield false test results. Training in specimen collection is highly recommended due to the importance of specimen quality. CLSI MM13 (Clinical and Laboratory Standards Institute) may be referenced as an appropriate resource.

- Refer to the UK Government guidance on handling and processing potential COVID-19 samples in laboratories: https://www.gov.uk/government/publications/wuhan-novel-coronavirus-guidance-for-clinical-diagnostic-laboratories/wuhan-novel-coronavirus-handling-and-processing-of-laboratory-specimens

- Refer to the World Health Organization Interim guidance on laboratory biosafety from 13 May 2020: Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance

- Refer to Interim Guidelines for Collecting, Handling and Testing Clinical Specimens from Persons under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19) https://www.cdc.gov/coronavirus/2019-nCoV/guidelines-clinical-specimens.html

- Follow specimen collection devices manufacturer instructions for proper collection methods.

- Swab specimens should be collected using swabs with a synthetic tip, such as nylon or Dracon® and with an aluminum or plastic shaft. Calcium alginate swabs are unacceptable and cotton swabs with wooden shafts are not recommended. Place swabs immediately into sterile tubes containing 2-3 ml of viral transport medium.

12.2 Transporting Specimens

- Specimens must be package, shipped and transported according to the current edition of the International Air Transport Association (IATA) Dangerous Goods Regulation. Follow shipping regulations for UN 3373 Biological Substance, Category B when sending potential SARS-CoV-2 specimens.

12.3 Storing Specimens

- Extracted nucleic acid should be stored at -70ºC or lower.
- Refer to **Section 12.1** weblinks for guidance

13. Reagent and Controls Preparation

13.1 Oasig™ OneStep 2x RT-qPCR Master Mix (lyophilized) preparation

- Upon receipt, the dried master mix can be stored at -20ºC for up to 18 months or the expiry date, whichever occurs first.
- Using aseptic technique, resuspend in 525µl of oasig™ resuspension buffer, gently swirl to mix.
- Store at -20ºC. Resuspended master mix is stable for up to six months when stored at -20ºC.
- Freeze/ thaw cycles should be minimized and not exceed 5 freeze/thaws. The reagent once resuspended can be aliquoted into smaller volumes if required and stored at -20ºC.

13.2 COVID-19 and IEC Primer/Probe mix preparation

- Upon receipt, the dried primers/probes mix can be stored at -20ºC for up to 18 months or the expiry date, whichever occurs first.
- Precautions: this reagent should only be handled in a clean area and not exposed to light.
- Using aseptic technique, resuspend the dried reagent in 110µl (per each vial) of Template preparation buffer and vortex to mix.
- Store at -20ºC. Resuspended primer/probe mix is stable for up to six months when stored at -20ºC.
- Freeze/ thaw cycles should be minimized and not exceed 5 freeze/thaws. The reagent once resuspended can be aliquoted into smaller volumes if required and stored at -20ºC.
- Store aliquots in the dark and keep away from exposed sunlight.

13.3 genesig® COVID-19 Positive control template preparation

- The genesig® COVID-19 Positive control template (PCT) is provided in a sealed foil envelope and contains a high copy number of templates. It should be opened and processed away from clinical specimens and kit components to avoid cross-contamination.
- The PCT tube contains synthetic DNA representing the SARS-CoV-2 genomic region of interest. Following resuspension, this will be at a concentration of 1.7×10^5 copies per µl.
- Caution: This reagent contains a high copy number of positive control material and should be handled with caution in a dedicated nucleic acid handling area to prevent possible contamination of other kit reagents and clinical specimens.
- Upon receipt, the dried PCT can be stored at -20ºC for up to 18 months or the expiry date, whichever occurs first.
- Using aseptic technique, resuspend the dried PCT in 600µl of Template preparation buffer, mix gently. Resuspended PCT is stable for up to six months when stored at -20ºC.
- Freeze/ thaw cycles should be minimized and not exceed 5 freeze/thaws. The reagent once resuspended can be aliquoted into smaller volumes if required and stored at -20ºC.
- To ensure PCR run validity, the PCT should produce amplification in the FAM channel.

13.4 genesig® Easy RNA Internal extraction control (IEC) preparation

- The genesig® Easy RNA Internal extraction control (IEC) can be added to the nucleic acid extraction system (not provided) to provide an RNA template control, detect PCR inhibition and confirm the integrity of the PCR run.
- Precautions: This reagent should be handled with caution in a dedicated nucleic acid handling area to prevent possible contamination.
- Upon receipt, the dried IEC can be stored at -20ºC for up to 18 months or the expiry date, whichever occurs first.
- Using aseptic technique, resuspend the dried IEC in 1000µl of Template preparation buffer, mix gently. Resuspended IEC is stable for up to six months when stored at -20ºC.
- Freeze/ thaw cycles should be minimized and not exceed 5 freeze/thaws. The reagent once resuspended can be aliquoted into smaller volumes if required and stored at -20ºC.

13.5 Negative Extraction Control (NEC) preparation

- Prepare at least 1 negative extraction control (NEC) each time RNA is extracted from a clinical specimen or sample.
- The NEC is an extraction with no clinical specimen/sample added, it is prepared by extracting from RNase/DNase free water. The IEC is added to the NEC sample during extraction as directed by the manufacturer's IFU. This NEC will serve as the negative control for the entire testing system and to check for contamination during PCR plate set-up.

13.6 No Template Control

- DNase/RNase free water is a provided to use as a No Template control (NTC) if required in addition to the NEC (refer to **Section 13.5)**
- The NTC is used to check for contamination during PCR plate set-up.

14. General Preparation

14.1 Equipment Preparation

- Clean and decontaminate all work surfaces, pipettes, centrifuges, and other equipment prior to use.
- Decontamination agents should be used such as 10% bleach, 70% ethanol, and an RNA/DNA remover to minimize the risk of nucleic acid contamination.
- Performance of the genesig® Real-Time PCR COVID-19 (CE IVD) assay is dependent upon the amount and quality of RNA purified from human specimens. The following commercially available RNA extraction kits and procedures have been validated for recovery and purity of RNA for use with this assay:
    - Automated extraction system GenoXtract® from HAIN Lifescience GmbH (Brucker) using the GXT NA Extraction kit.
    - Qiagen extraction system with QIAamp® Viral RNA Mini kit (Qiagen, Germany)
    - exsig™ Mag extraction kit with Kingfisher Flex

Manufacturer's recommended procedures are to be followed for sample extraction.

15. Assay Set Up

15.1 Sample Preparation Procedure

Prepare at least 1 negative extraction control (NEC) each time an extraction is performed (i.e. an extraction with no clinical specimen/sample added). This NEC will serve as the negative control for the entire testing system.

	Nasopharyngeal swabs, oropharyngeal swabs, sputum*	Saliva****
Collection	Swabs: Dacron or polyester flocked swabs in viral transport medium Sputum: Viral transport medium in sterile container	sterile container
Transport temperature**	2-8ºC ≤ 72hrs	≤-20˚C
Short-term storage (pre-extraction) **	2-8ºC ≤ 72hrs	≤-20˚C up to 3 months
Long-term storage (pre-extraction) **	≤ -70˚C for longer periods	≤ −80 ˚C
Extraction sample volume	700µL***	700µL***
Extraction elution volume	85µL	85µL

*Sputum must be from the lower respiratory tract
**These are CDC recommendations: CDC Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with SARS-CoV-2
https://www.cdc.gov/coronavirus/2019-nCoV/lab-biosafety-guidelines.html
***Sample refers to the viral transport medium provided in the sample container serving as the repository for the swab.
**** For saliva specimen storage please refer to BSI Guidelines PD CEN/TS 17305:2019.
Local regulations pertaining to sample handling may also apply.

15.2 RNA extraction

The results of the genesig® Real-Time PCR COVID-19 (CE IVD) assay is dependent upon the amount and quality of template RNA purified from human specimens.

- Consult the IFU of the extraction system for full usage details.
- Prepare at least 1 negative extraction control (NEC) each time an extraction is performed (i.e. an extraction with no clinical specimen/sample added).
- The genesig® Easy RNA Internal extraction control (IEC) should be resuspended in 1000µl template preparation buffer. It should be incorporated in the extraction as directed by the extraction system IFU. Primerdesign recommends 20µl is added per sample, directly into the lysis stage of the extraction.

The internal extraction control should not be added directly to the clinical specimen/ sample before RNA extraction (i.e. not before the clinical specimen/sample is mixed with a lysis buffer of the nucleic acid extraction kit/system). Doing so may compromise the testing.

- Where the IFU provides no specific guidance for the addition of an Internal extraction control or where an automated system does not support the addition of 20µl IEC, please contact Primerdesign for guidance.

15.3 Master Mix Setup

a) Resuspend the COVID-19/IEC primer/probe tube in template preparation buffer, 110µl of buffer per tube, vortex to mix.
b) Resuspend the oasig™ OneStep 2X RT-qPCR Master Mix in 525µl oasig™ resuspension buffer, gently swirl to mix.
c) Plate set-up configuration can vary with the number of specimens. An NEC must be included in each plate set-up (refer to **Section 13.5 and 15.2** on how to prepare NEC). NTCs should be included in each plate set-up. A PCT must be included in each plate set-up.
    a. The PCT will be added after all other reagents and samples have been added to the plate.
    b. This will be in an area for handling nucleic acid and away from the NEC, NTC and any clinical specimen/ samples.
    c. This is to prevent plate set-up, reagent or specimen contamination with the PCT.
d) Determine the number of reactions (n) to set up per assay (including NEC, PCT and any NTCs for each plate). It is necessary to make excess reaction mix to allow for pipetting error. Use the following guide to determine volume of reagents to add to the reaction mix:
    1. If number of samples (n) is ≤ 10, then N = n+1
    2. If number of samples (n) is > 10 and ≤ 20, then N = n+2
    3. If number of samples (n) is > 20, then N = n+ 10% of total number of samples

e) Prepare a reaction mix of the following reagents from resuspended components in a 1.5ml DNase/RNase free tube:

Reaction mix Component	1 x volume required (µl) *
Oasig™ OneStep 2X RT-qPCR Master Mix	10*
COVID-19 and IEC Primer & Probe	2*

*Multiply all numbers by (N). Refer to step (d) above, to ensure there is sufficient reaction mix for all samples, NEC, PCT and NTCs to be tested.

f) Add 12µl into the number of wells required for your testing, in an appropriate 96 well plate for your chosen PCR platform. Include 1 well for the PCT, 1 well for the NEC and 1 well for the NTC for each PCR plate.
g) Add 8µl of the following into the appropriate wells according to your plate setup:
    a. NEC (please refer to **Sections 13.5**)
    b. NTC (please refer to **Sections 13.6**)
h) Cover the entire reaction plate and move the reaction plate to the specimen nucleic acid handling area.
i) Gently vortex nucleic acid sample tubes for approximately 5 seconds.
j) Centrifuge for 5 seconds to collect contents at the bottom of the tube, and then place the tube

in a cold rack.

k) Change gloves often and when necessary to avoid contamination.
l) Add 8µl of the RNA/nucleic acid extracted from clinical specimen/sample(s) into the appropriate wells according to your plate setup.
m) Cover the entire reaction plate and move the reaction plate to the positive template control handling area.
n) Add 8µl of PCT (please refer to **Sections 13.3**) into the appropriate well according to your plate set up. Seal the plate with an appropriate seal and place in the instrument.

15.4 Programming the Real-Time PCR Instrument

Please refer to one of the following manuals for additional information on using the instrument:

- Applied Biosystems® 7500 Real-Time PCR system Relative Standard curve and comparative CT Experiments (as per Applied Biosystems manual (2010)).
- LightCycler 480 instrument Operator's manual (July 2016, Addendum 4, Software version 1.5)
- Bio-Rad CFX Connect™ Real-Time PCR Detection System Instrument Guide (as per Bio-Rad Laboratories Inc. Manual (2017))
- FluoroCycler® XT (FC XT 101, Bruker Hain Lifescience)
- QuantStudio 5 (ThermoFisher Scientific, QuantStudio Design & Analysis Software v 1.4.3)

a) Enter the following amplification program:

Steps	Time	Temperature	Cycles	Detection Format
Reverse Transcription	10 min	55˚C	1	COVID-19 = FAM (465-510) RNA Internal Extraction Control (IEC) = VIC / HEX / Yellow555 (533-580)
Initial Denaturation (Taq Activation)	2 min	95˚C	1	
Denaturation	10 sec.	95˚C	45	
Annealing and Extension	60 sec.	60˚C*		

*Acquisition must be performed at the end of this stage
When using Roche® LightCycler 480 II please select the following detection format: Dual Color Hydrolysis Probe / UPL Probe
When using the ABI 7500® please select 'none' for the dye to use as passive reference dye in the plate set up

b) Ensure wells loaded with clinical sample(s) are designated as "Sample Type – Unknown"
c) Ensure the well loaded with PCT is designated as "Sample Type – Positive Control"

16. Interpretation of Results

16.1 Acceptance Criteria of controls included in the genesig® Real-Time PCR COVID-19 (CE IVD) assay

Before interpreting sample results, it is necessary to verify the success of the run. If the following criteria are not satisfied, then testing needs to be repeated:

a) NEC is free from amplification in the FAM (465-510) channel and NEC produces positive amplification in the VIC/HEX/Yellow555 (533-580) channel (this is detection of the genesig® Easy RNA Internal Extraction control).
b) PCT produces a Cq of between 14-22 in the FAM (465-510) channel.

For instrument specific guidance on correctly assigning Cq values follow manufacture instructions.

Please manually inspect amplification curves for all samples assigned a Cq value to verify the positive amplification.

16.2 Interpretation of Patient Specimen Results

If all the control acceptance criteria are fulfilled, then each sample can be assessed with the following metric:

		SARS-CoV-2 Target (FAM (465-510))	
		Cq Positive	Cq Negative
IEC (VIC / HEX / Yellow555 (533-580))	Cq Positive	SARS-CoV-2 Positive*	SARS-CoV-2 Negative**
	Cq Negative	SARS-CoV-2 Positive*	Result invalid Repeat testing of sample

*All instances of test sample amplification in the FAM channel indicate a SARS-CoV-2 positive sample. Please manually inspect amplification curves for all samples assigned a Cq value to verify the positive amplification.

**If there is no amplification in the FAM channel for a test sample, to confirm the FAM result is valid as SARS-CoV-2 negative, there should be amplification in the VIC/HEX channel. This confirms the PCR run is valid and the genesig® Easy RNA IEC added to the test sample during the RNA extraction process has been detected. The following acceptance criteria should be applied for FAM negative samples:

- The IEC Cq value produced by the patient sample should be < 36 and should not exceed the NEC IEC Cq value + 6 (i.e. sample RNA IEC Cq < NEC RNA IEC Cq + 6). Failure to satisfy this criterion indicates a compromised sample extraction and an invalid result; testing of the sample must be repeated.

17. Limitations of The Procedure

- The procedures in this handbook must be followed as described. Any deviations may result in assay failure or cause erroneous results.
- Good laboratory practice is required to ensure the performance of the kit, with care required to prevent contamination of the kit components. Components should be monitored for contamination and any components thought to have become contaminated should be discarded as standard laboratory waste in a sealed pouch or zip-lock plastic bag.
- As with any molecular test, mutations within the target sequence of SARS-CoV-2 could affect the genesig® COVID-19 primer and/or probe binding, resulting in failure to detect the presence of the virus.
- False negative results may be caused by:
    - Unsuitable collection, handling and/or storage of samples.
    - Sample outside of viraemic phase.
    - Failure to follow procedures in this handbook.
    - Use of unauthorised extraction kit or PCR platform.
- False positive results may be caused by:
    - Unsuitable handling of samples containing high concentration of SARS-CoV-2 viral RNA or positive control template.
    - Unsuitable handling of amplified product.
- All results should be interpreted by a health care professional in the context of patient medical history and clinical symptoms.
- This test cannot rule out diseases caused by other pathogens.
- A negative result for any PCR test does not conclusively rule out the possibility of infection.

18. Performance Evaluation

The genesig® Real-Time PCR COVID-19 (CE IVD) assay performance evaluation has been generated on the Applied Biosystems® 7500 Real-Time PCR system with additional testing on the Roche® LightCycler 480 II and Bio-Rad CFX Connect™ Real-Time PCR Detection System instruments for analytical sensitivity (LoD). A set of additional testing at the LoD level has been performed for the additional qPCR instruments and extraction systems listed in **Sections 7 and 8**.

18.1 Analytical Sensitivity

The Limit of detection (LoD) is defined as the lowest concentration of analyte that could be reliably detected at least 95% of the time. First a tentative LoD was assessed by testing five contrivance levels (dilutions) of SARS-CoV-2 whole viral RNA spiked into five samples negative for SARS-CoV-2. Once the tentative LoD was established it was confirmed by testing 20 additional contrived samples negative for SARS-CoV-2.
LoD level was established using oropharyngeal swabs, nasopharyngeal swabs and saliva specimen using SARS-CoV-2 whole viral RNA supplied by the European Virus Archive-Global (EVAg) or by ®Twist Bioscience.
Samples were extracted with the GXT DNA/RNA Extraction kit on the Automated GenoXtract® system (Bruker HAIN Lifescience). The LoD results are described in **Sections 18.1.1, 18.1.2 and 18.1.3**.

18.1.1 Analytical Sensitivity Results

The LoD was confirmed by testing 20 oropharyngeal samples negative for SARS-CoV-2 contrived with of SARS-CoV-2 whole viral RNA supplied by EVAg at a selected contrivance level. Samples were extracted with the GXT DNA/RNA Extraction kit on the Automated GenoXtract® system (Bruker HAIN Lifescience) and tested on the Applied Biosystems® 7500 Real-Time PCR System.
The LoD was further confirmed by testing 20 nasopharyngeal swabs and 20 saliva samples contrived with SARS-CoV-2 whole genomic RNA supplied by ®Twist Bioscience; samples were extracted with the GXT NA Extraction kit on the Automated GenoXtract® system (Bruker HAIN Lifescience) and tested on the Applied Biosystems® 7500 Real-Time PCR System:

	Applied Biosystems® 7500 Real-Time PCR System					
Sample type	**SARS-CoV-2 Mean Concentration (copies/µl)**	**Overall Mean Concentration (copies/rxn)**	**Positive calls/Total no. results included in analysis**	**% Replicate Detection**	**Mean Cq**	**Cq Standard Deviation**
Oropharyngeal swab	0.33	2.65	20/20	100	36.3	0.967
Nasopharyngeal swabs	0.18	1.44	20/20	100	37.9	0.81
Saliva	0.28	2.24	20/20	100	37.1	0.73

This data demonstrates that the genesig® Real-Time PCR COVID-19 (CE IVD) assay detects ≤ 0.33 copies/µl of SARS-CoV-2 whole viral genome RNA ≥95% of the time. This concentration therefore is the limit of detection of the assay.

18.1.2 Alternative Instrument Testing

The LoD was further confirmed by testing 20 contrived samples (oropharyngeal swabs contrived with SARS-CoV-2 whole genomic RNA supplied by EVAg) on the **CFX Connect™ Real-Time PCR Detection System (Bio-Rad) and LightCycler 480 II (Roche®) qPCR:**

PCR Instrument	Positive calls/Total no. results included in analysis	% Calls	Mean Cq	Overall Mean Concentration (copies/µl)	Overall Mean Concentration (copies/rxn)	Cq Standard Deviation
CFX Connect™ Real-Time PCR	20/20	100	36.8	0.29	2.34	1.436
LightCycler 480 II qPCR	20/20	100	37.7	0.18	1.41	1.050

FluoroCycler® XT real time PCR instrument (Bruker Hain Lifescience) has been validated using GXT NA Extraction kit and Automated GenoXtract® system (Bruker HAIN Lifescience) using 20 negative oropharyngeal swabs contrived with SARS-CoV-2 whole genomic RNA supplied by EVAg**:**

PCR Instrument	Positive calls/Total no. results included in analysis	% Calls	Overall Mean Concentration (copies/µl)	Overall Mean Concentration (copies/rxn)
FluoroCycler® XT Real-Time PCR	19/20	95	0.36	2.88

QuantStudio 5 Real-Time PCR System (ThermoFisher Scientific) has been validated by Hammersmith Medicines Research Ltd by testing contrived samples (oropharengeal swabs) using a known copy number synthetic RNA template representing the SARS-CoV-2 genomic region of interest. Samples were extracted with the QIAamp® viral RNA mini kit, 20 replicates were tested on the QuantStudio 5 Real-Time PCR System.

PCR Instrument	Positive calls/Total no. results included in analysis	% Calls	Overall Mean Concentration (copies/µl)	Overall Mean Concentration (copies/rxn)
QuantStudio 5 Real-Time PCR	19/20	95	0.147	1.18

The lowest concentration that produced 95% replicate detection was 0.147 copies/ul (20/20 replicates) with mean Cq 37.68 (STDEV 1.15).

The results above confirm that LoD of 0.33 copies/µl is maintained across all PCR instruments tested when using GXT DNA/RNA Extraction kit, GXT NA Extraction Kit or QIAamp Viral RNA Mini kit.

18.1.3 exsig™ Mag extraction system

The LoD for the genesig® Real-Time PCR COVID-19 (CE IVD) assay was further confirmed by testing 20 contrived samples (oropharyngeal swabs contrived with SARS-CoV-2 whole genomic RNA supplied by ®Twist Bioscience) with **the Kingfisher Flex extraction system and the exsig Mag® extraction kit.** The tentative LoD was established by preparing 9 limiting dilutions (contrivance levels) of SARS-CoV-2 whole genomic RNA contrived into fifteen COVID-19 negative oropharyngeal swab samples. The claimed LoD was confirmed by testing thirty-six additional COVID-19 negative oropharyngeal swab samples contrived at the selected limiting dilution:

CFX Connect™ Real-Time PCR					
SARS-CoV-2 Mean Concentration (copies/µl)	Overall Mean Concentration (copies/rxn)	Positive calls/Total no. results included in analysis	% Replicate Detection	Mean Cq	Cq Standard Deviation
0.63	5.04	35/36	98%	36.21	0.46
0.18	1.44	**36/36**	**100%**	**38.13**	**0.94**
0.07	0.56	29/36	76%	39.94	0.91
0.069	0.55	18/36	50%	40.1	1.45

In this study, the LoD of 0.18 copies/µl was obtained and a level of confidence of >95% was maintained when using the genesig® Real-Time PCR COVID-19 (CE IVD) assay in combination with the Kingfisher Flex and the exsig™ Mag extraction kit.

18.2 Inclusivity

18.2.1 Latest in silico Specificity Analysis:

To ensure the COVID-19 primers and probe remain specific to detect SARS-CoV-2 genomes, Primerdesign's Bioinformaticians review daily the SARS-CoV-2 sequence submissions on the GISAID EpiCoV database. As of 17th of May 2020, *in silico* analysis confirms the COVID-19 assay primers and probe still show 100% detection with the 42,655 full length, good quality SARS-CoV-2 sequences published on the GISAID EpiCoV database.

18.2.2 Analytical Specificity

Related Pathogens and pathogens that are likely to be present in the clinical specimen have been evaluated *in silico* to identify the homology between the primers/probe of the assay and the pathogens. Upon *in silico* analysis, the genesig® Real-Time PCR COVID-19 (CE IVD) assay exhibited no cross-reactivity with non-SARS-CoV-2 species except for two sequences, Bat coronavirus (NCBI Accession No. MN996532.1) and Pangolin coronavirus (NCBI Accession No. MT084071.1) sequences. The primers/probe sequence has 5 mismatches and 7 mismatches respectively, with these viruses and therefore show limited possibility of being detected with the genesig® Real-Time PCR COVID-19 (CE IVD) assay.

In vitro testing:
For *in vitro* testing, 4 panels were sourced:

- Respiratory Evaluation Panel (Qnostics, Scotland, UK)
- QCMD panel from the 2019 Coronavirus EQA programme (Qnostics)
- Respiratory validation panel (ZeptoMetrix)
- Pneumonia Validation panel (ZeptoMetrix)

The samples from these panels are representative of true clinical human specimens and evaluated by the COVID-19 genesig® Real-Time PCR assay in triplicates. The results of the *in vitro* cross-reactivity testing are presented below:

Virus	Strain	Source	Detected/Replicates	Final result
INF A H1N1 positive	-	Isolate	0/3	Negative
INF A H3N2 positive	-	Isolate	0/3	Negative
INF B Victoria	-	Isolate	0/3	Negative
INF B Yamagata	-	isolate	0/3	Negative
RSV A	-	isolate	0/3	Negative
RSV B	-	isolate	0/3	Negative
Coronavirus	NL63	isolate	0/3	Negative
Coronavirus	229E	isolate	0/3	Negative
Coronavirus	HKU	isolate	0/3	Negative
Coronavirus	OC43	isolate	0/3	Negative
Influenza AH1	-	isolate	0/3	Negative

Virus	Strain	Source	Detected/Replicates	Final result
Influenza AH3	-	isolate	0/3	Negative
Influenza B		isolate	0/3	Negative
Metapneumovirus	-	isolate	0/3	Negative
Enterovirus	-	isolate	0/3	Negative
Adenovirus 3	-	isolate	0/3	Negative
Parainfluenza 3	-	isolate	0/3	Negative
Rhinovirus	-	isolate	0/3	Negative
S. pyogenes	Z018	isolate	0/3	Negative
Parainfluenza 2	-	isolate	0/3	Negative
S. pneumoniae	Z022	isolate	0/3	Negative
S. marcescens	Z053	isolate	0/3	Negative
S. aureus	MRSA, COL	isolate	0/3	Negative
S. agalactiae	Z019	isolate	0/3	Negative
K. pneumoniae	Z460; NDM-1	isolate	0/3	Negative
Coronavirus SARS	-	isolate	0/3	Negative
Parainfluenza	-	isolate	0/3	Negative
K. pneumoniae	Z138	isolate	0/3	Negative
K. pneumoniae	Z460	isolate	0/3	Negative
P. aeruginosa	Z139, VIM1	isolate	0/3	Negative
P. mirabilis	Z050	isolate	0/3	Negative
K. aerogenes	Z052	isolate	0/3	Negative
H. influenzae	MinnA	isolate	0/3	Negative
E. coli	Z297	isolate	0/3	Negative
E. cloacae	Z101	isolate	0/3	Negative
A. baumannii	307-0294	isolate	0/3	Negative

18.3 Precision

Assessment of repeatability (intra-run) and reproducibility (inter-run) of the genesig® Real-Time PCR COVID-19 assay has been performed by contriving SARS-CoV-2 negative oropharyngeal swab samples with a known copy number synthetic RNA template representing the SARS-CoV-2 genomic region of interest at two contrivance levels* (reproducing a medium and low viral load samples):

- Medium viral load sample: 1.06 x 10^4 copies/ml
- Low viral load sample: 5.30 x 10^3 copies/ml

*Contrivance level concentrations were based on analytical sensitivity of the assay in **Sections 18.1.1 and 18.1.2.**

Samples were extracted with the GXT DNA/RNA Extraction kit on the Automated GenoXtract® system (Bruker HAIN Lifescience) and tested on the Applied Biosystems® ABI 7500 Real Time PCR system.

Variance was assessed from operators, instruments, and day of test: 2 different operators performed the study over 3 days, with two Applied Biosystems® ABI 7500 Real Time PCR instruments.

A total of 36 replicates were obtained for each contrivance level (medium and low viral load sample).

The precision was measured by reporting the Coefficient of Variance which were well below an accepted industrial standard of 9% for all studies:

Summary of Repeatability and Reproducibility for the genesig® Real-Time PCR COVID-19 CE IVD assay (FAM and VIC channels)

	Coefficient of variance (%) for COVID-19 (CE-IVD) genesig® Real-Time PCR assay (FAM)			
Sample concentration (copies /ml)	Repeatability	Inter-Instrument	Inter-operator	Inter-day
1.06×10^4	0.77	4.94	2.75	3.98
5.30×10^3	1.55	5.22	2.83	3.99

	Coefficient of variance (%) for COVID-19 (CE-IVD) genesig® Real-Time PCR assay (VIC)			
Sample concentration (copies /ml)	Repeatability	Inter-Instrument	Inter-operator	Inter-day
1.06×10^4	0.87	2.12	1.02	1.87
5.30×10^3	1.09	2.02	1.08	1.86

18.4 Clinical Performance Evaluation

Clinical evaluation of the genesig® Real-Time PCR COVID-19 (CE IVD) assay was conducted with contrived oropharyngeal swabs (50 positive and 50 negative) in Copan universal transport medium. 50 swabs were contrived with SARS-CoV-2 whole viral genomic RNA (EVAg, Cat: 026N-03889) and tested blindly to generate the Positive Percentage Agreement (PPA) and Negative Percentage Agreement (NPA):

SARS-CoV-2 concentration	Results (Detected /Tested)	genesig® Real-Time PCR COVID-19 (CE IVD) assay % Positive (95% CIs)
1-2x LoD	36/38	94.7% (82.72 - 98.55)
3x LoD	7/7	100% (64.57 - 100)
4-5x LoD	5/5	100% (56.56 - 100)
Negative	50/50	100% (92.87 - 100)

Independent Clinical Performance testing

57 patient combined nose and throat swabs were evaluated by Hampshire Hospitals NHS Foundation Trust throughout February and early March 2020. The genesig® Real Time PCR COVID-19 (CE IVD) assay detected all known true positive (4 samples) and true negative (53 samples) clinical patient samples confirming the assay has 100% specificity for SARS-CoV-2 virus.

195 specimens including upper or lower respiratory clinical specimens negative were evaluated by National Infection Service, Public Health England (PHE), Colindale. Statistical assessment of the panel size determined that when the measured specificity for this sample size is 100% that the true specificity of the COVID-19 genesig® Real-Time PCR assay was at least 98.2%.

Summary for Independent Clinical Performance and Accuracy results for the genesig® Real Time PCR COVID-19 (CE IVD) assay are shown below:

Diagnostic test	Assessed by	Samples number	True Positive	False Positive	True Negative	False Negative	Positive % agreement	Negative % agreement
genesig® Real-Time PCR COVID-19 (CE IVD)	1. National Infection Service, Public Health England, Colindale	195	0*	0	195	0	N/A	100%
	2.Hampshire Hospitals NHS Foundation Trust	57	4	0	53	0	100%	100%

- **PHE assessed the assay with known SARS-CoV-2 positive material and confirmed all known SARS-CoV-2 samples were detected, even after a three-step dilution series. True Positive and True negative as defined by Public Health England*

19. Disposal

Dispose of unused kit reagents, human specimens and sealed post-amplification plates as laboratory clinical waste according to local, state and federal regulations. Refer to **Section 12** for guidance weblinks

20. Primerdesign Ltd Quality Control

In accordance with Primerdesign Ltd ISO 13485 certified Quality Management System, each batch of the genesig® Real-Time PCR COVID-19 (CE IVD) assay is tested against predetermined specifications to ensure consistent product quality.

Primerdesign Ltd perform weekly *in silico* analysis of all published SARS-CoV-2 genomes (GISAID EpiCoV and NCBI databases) to identify if the virus mutates in the COVID-19 primer and probe target region.

21. Verification Requirements for genesig® Real-Time PCR COVID-19 (CE IVD) assay

21.1 SARS-CoV-2 RNA Verification Process

- Purified SARS-Cov-2 whole viral RNA listed below is an example of a verification material. Laboratories can use other available appropriate materials to verify the genesig® Real-Time PCR COVID-19 (CE IVD) assay.
- SARS-CoV-2 whole viral RNA supplied by EVAg (Cat: 026N-03889) was used for this process. This SARS-CoV-2 RNA is purified from a cell culture of the Coronavirus strain "BetaCoV/Germany/BavPat1/2020 p.1".
- The estimated concentration of this material is 10^4 copies/µl. It should be opened and processed away from clinical specimens and kit components to avoid cross-contamination.
- Users are required to verify the SARS-Cov-2 whole viral RNA by preparing a four-point standard curve of three 1:10 serial dilutions down to 10 copies/µl:
    i) Label 3 x 1.5ml microcentrifuge tubes with the SARS-CoV-2 RNA concentration:
        - 10^3 copies/µl
        - 10^2 copies/µl
        - 10 copies/µl.
    ii) Pipette 90µl of RNase/DNase-free water into each labelled 1.5 ml microcentrifuge tubes.
    iii) Very briefly vortex and centrifuge SARS-CoV-2 RNA.
    iv) Perform a 1/10 dilution by transferring 10µl of the neat SARS-CoV-2 RNA into 10^3 copies/µl tube. Vortex briefly, change pipette tip.
    v) Perform a 1/10 dilution by transferring 10µl of 10^3 copies/µl tube into 10^2 copies/µl. Vortex briefly, change pipette tip.
    vi) Perform a 1/10 dilution by transferring 10µl of 10^2 copies/µl tube into 10 copies/µl. Vortex briefly.
- Prepare a reaction mix according to **Section 15.3**, ensure enough reaction mix is prepared for a single replicate of a positive control, a negative control and testing each dilution of the SARS-CoV-2 RNA in triplicate.
- Prepare a reaction plate according to **Section 15.3** and program your chosen PCR platform according to **Section 15.4.**
- Before interpreting the results, ensure that the following criteria is met:
    - NTC is free from amplification in the FAM (465-510) channel
    - PCT produces amplification in the FAM (465-510) channel
- All SARS-Cov-2 RNA reference material tested concentrations should produce amplification through the FAM channel.

22. Technical Support

For Technical support, please contact our dedicated technical support team on:

Phone: +44 (0) 800 0156 494

Email: support@primerdesign.co.uk

23. Trademarks and Disclaimers

Trademarks: exsig™, oasig™, genesig® and the Primerdesign logo.

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24. Explanation of Symbols

Symbol	Explanation
	In vitro diagnostics
	Manufacturer
	Catalogue number
	Sufficient for number of tests
	Use by Date
	Temperature limit
	Consult Electronic Instructions for Use
	Batch Code
	Keep away from sunlight (primer/probe mix)
	Positive Control

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