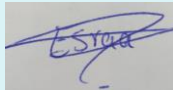






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POLICY PROCEDURE FOR COVID 19 NUCLEIC ACID EXTRACTION

	NAME	DESIGNATION	SIGNATURE	DATE
Prepared by	Esraa Hamid	QUALITY OFFICER		25/07/2020
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1 REVISION HISTORY

#	Version	Date	Changes Made by	Reason for Changes	Clause Changed
1	2	15/07/2020	Quality department	Method of adding positive control	9.13.2.





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2 REVIEW HISTORY

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1	1.0				





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3 POLICY STATEMENT

This policy describes the procedure of the nucleic acid extraction of SARS-Covid Nucleic Acid Detection.

4 PURPOSE

COVID-19 Nucleic Acid Detection (RT-PCR).

5 SCOPE

The policy is applicable to SARS-Cov-2 nucleic acid detection (RT-PCR fluorescence probe method).

6 DEFINITIONS

Nil

7 ACRONYMS

7.1	COVID-19:	CORONAVIRUS DISEASE 2019
7.2	SARS-COV-2:	SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2
7.3	Real time RT-PCR:	Real-time reverse transcriptase polymerase chain reaction.
7.4	BSC:	Biological safety Cabinet
7.5	Ct value:	cycle threshold
7.6	VIC/HEX:	Human House-keeping gene β -actin for control with HEX/VIC channel
7.7	FAM:	COVID 19 specific gene ORF-1ab for SARS-CoV-2 with FAM channel
7.8	PBS:	Phosphate-buffered saline or solution
7.9	Bp :	Base pair
7.10	ng:	nanogram
7.11	Rxn:	Reagent
7.12	MLB:	magnetic lysate buffer
7.13	MW1:	molecular wash 1





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- 7.14 MW2: molecular wash 2
7.15 NF: Nuclease free water
7.16 UV: Ultraviolet radiation

8 RESPONSIBILITIES

- 8.1. Laboratory director
- 8.2. Laboratory Deputy Director
- 8.3. Quality Manager
- 8.4. Quality Officer
- 8.5. Infection control officer
- 8.6. Medical laboratory technologist

9 PROCEDURE

9.1 Safety Precaution:

9.1.1. Safety and precaution:

You can enter the laboratory after fully dressing in the dressing room (PPE). The specific dressing order is: disposable cap → N95 mask → protective clothing → shoe cover → sleeve → three latex gloves → face shield.

9.2. Method:

The total RNA of the sample was extracted and transcribed into mRNA as template. Oligo (dT) or random primers were used to realize the reverse-transcription into cDNA with reverse transcriptase. cDNA product serve as a template for PCR amplification during which the fluorescence signal is collected.





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9.3. TEST PRINCIPLE:

The kit is based on in vitro RT-PCR combining fluorescent probing. Primers and a sequence-specific fluorescence probes were designed tailored to the high conservative region of SARS-Cov-2 genome. The probes are oligonucleotide attached fluorophores at the 5' end with FAM as reporter and 3' end with quencher. In a meantime, specific primers and probes were developed as internal reference with fluorophores VIC/HEX attached at 5' end as reporter.

During the PCR procedures, the DNA polymerase cleaves the probes at the 5' end and separates the reporter dye from the quencher dye when the probes hybridize to the target DNA. This cleavage results in the fluorescent signal generated by the cleaved reporter dye, which is monitored in real-time by the PCR detection system. Monitoring the fluorescence intensities in real time allows the qualitative detection of SARS-Cov-2 in specimens.

9.4. PERFORMANCE CHARACTERISTICS:

9.4.1. This test is verified with (accuracy, precision, carryover).

9.4.2. Limit of detection of the QPCR kit is 100 copies /ml for detecting 2019-nCov

9.4.3. positive control is positive at both FAM/ and VIC channel while the blank control is negative at both channel

9.4.4.A potential cross -reactivity of the RT-PCR kit was tested and none of the tested pathogen have been reactive

9.4.5. Repeatability

9.4.6. Reproducibility

9.5. TYPE OF SAMPLE/CONTAINER/ADDITIVE/PATIENT PREPARATION:

9.5.1. Sample type, Storage, and Stability:

Use only nasopharyngeal swab with transport media as specimen for the test.

9.5.2. Sample storage and stability:

9.5.2.1. short storage at -20 °C as per sample retention policy





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9.5.2.2. Long storage at -80 °C avoid repeat freezing and thawing it will effect on the quality of the sample and the result

9.5.3. Container/ Additives:

Nasopharyngeal swabs (NPS) or nasal swab (NS) in Copan universal transport media (UTM OR BD UNIVERSAL VIRAL TRANSPOT

9.5.4. Handling of Specimens:

9.5.4.1. Make sure the sample is sufficient

9.5.4.2. Adequate mixing of sample and vortex

9.5.4.3 Error in patient and/or specimen identification

9.5.4.4. Adequate specimen storage conditions

9.5.4.5. Perform the test as soon as possible

9.6. Patient Preparation:

No special patient preparation required for the test.

9.7. Sample acceptance and rejection criteria:

9.7.1 Acceptance Criteria:

Sample of nasopharyngeal swab with transport media or throat swab sample

9.7.2 Rejection Criteria:

Leakage sample, Incorrect volume of sample and insufficient sample





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9.8. REQUIRED EQUIPMENT AND REAGENT:

9.8.1. Instruments:

9.8.1.1. Biosafety cabinet class B2: use for sample receiving and dispensing area to prepare the plate.

9.8.1.2. High speed centrifuge: Eppendorf tubes centrifuging.

9.8.1.3. Hand centrifuge: use for 96 well plate centrifuging.

9.8.1.4. Pipette: use for Samples a liquating

- Single channel pipette.
- Multi-channel pipette: for R- QPCR preparation .

9.8.1.5. Vortex: use Mixing the samples.

9.8.1.6. Temperature and humidity indicator: Monitoring temperature and humidity

9.8.1.7. Dry mist hydrogen peroxide sterilizer: Laboratory disinfection

9.8.1.8. Automated sample preparation system (MGISP-960RS): RNA extraction

9.9. Reagent:

No.	Reagent name	Usage	Storage and stability
1	NF (Nuclease Acid Free Water)	Washing Buffer	Room temp (on board)
2	MW 1 (Molecular Wash - 1)	Washing Buffer	Room Temp (on board)
3	MW2 (Molecular Wash -2)	Washing Buffer	Room Temp (on board)
4	MLB (Extraction Reagent)	Lysate & Binding Buffer	30 min 4C





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5	Q-PCR mix	Qualitative Nucleic acid Amplification	2 hr at – 20 C
6	Negative Control	DNAase /RNAase Free Water	-20 c for 6 month
7	Positive control	Mix solution of pseudo-virus gene and internal reference	-20 C for 6 month

9.10. Storage and Stability:

Status	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened	-20 °C	Until expiration date	Store in upright position.

Note:

Reagent must be stored as labeled to ensure optimal performance. any reagent exposed to temperature out said of labeling limits should not be used. reagent quality can be deteriorating with time; therefore, use all reagent before expiration date on the label, protect reagents from extreme heat freezing during storage.

9.11. Supplies:

9.11.1 Disposable gloves

9.11.2 Containers for infectious materials

9.11.3. Alcohol Wipes

9.12 ENVIRONMENT & SAFETY CONTROL:

9.12.1. Humidity / Temperature





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9.12.2. In vitro diagnostic use

9.12.3. Exercise the standard precautions required for handling all Laboratory reagents.

9.12.4. Disposal of all waste material in accordance with Procedure for Waste Management

9.12.5. Avoid the formation of foam with all reagents and sample types (specimens, and controls).

9.13. QUALITY CONTROL:

Before adding controls to the plate, be sure the vials have been properly warmed and mixed to room temperature (18 to 30 °C) for 15 minutes. Do NOT mix mechanically or vortex. Run the two of control (positive and blank control) with each plate

9.13.1 Blank Control:

9.13.1.1 The blank control it contains DNase /RNase free water, CT value at FAM &VIC /HEX channels are 0 or no data available

9.13.1.2. Add 160 ul on the C3 well before extraction procedure

9.13.2. Positive Control:

9.13.2.1. The positive control is mix of pseudo-virus with target virus and internal reference, standard curve at channel FAM& VIC /HEX channels are in S- shape with CT value not higher than 32

9.13.2.2. Add only 10 ul of the positive control into the QPCR-Mix plate, seal it fastened and centrifuge the plate at 2000 rpm for 10 seconds. Place the plate into thermocycler and record the exact location of controls and every specimen

9.14. Quality control:

required after a reagent lot number change





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9.15. PROCEDURE:

9.15.1. Environmental Control and Safety:

9.15.2. The laboratory environmental assessment is qualified;

9.15.3. After entering the laboratory, temperature and humidity of the laboratory should be checked and recorded (20 °C for freezer while 4 °C for refrigerator).

9.15.4. Laboratory temperature range: (20 °C ~ 25 °C).

9.15.7. Humidity range: (30% ~ 70%).

9.15.8. -20 °C freezer temperature range: (-15 °C ~ -25 °C).

9.15.9. Refrigerator temperature range: (2 °C ~ 8 °C)

9.16. Sample preparation:

Confirm the quantity of inactivated samples that transferred from the sample inactivation area. Fill the 《COVID-19 Inactivated Sample Delivery Record》 Vortex Samples, then stand for at least 10s.

9.17. Samples Arrangement:

Arrange a new plate task for samples using the Computer, the processes are as bellow:

Open the plate arrangement excel file 《COVID-19 Sample Nucleic Acid Test Record》, change the file name according to the experiment date in the format of "Year Month Day – X." (For example, 20200214-1, X=0、1、2、3...), and save as a new file; Arrange all samples in the 96-well plate, and empty C3, H12 for PBS, Blank Control, Positive Control respectively. Scan the sample ID according to the 96-well plates, to fill the content of "sample ID" column in excel file. When scan completed, check to confirm there is no repeat sample ID, if there is, the well will become into yellow background and black letter. All details are showed in the bellow Figure 1.





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 Document No: BG/REC/MOL/017 Version: 01												well	Sample ID		
COVID-19 Sample Nucleic Acid Test Record												A1			
Plate ID: _____						Arrange Staff: _____						Time: _____		B1	
Sample ID	1	2	3	4	5	6	7	8	9	10	11	12			
A	1 □	9 □	17 □	25 □	33 □	41 □	49 □	57 □	65 □	73 □	81 □	89 □			
B	2 □	10 □	18 □	26 □	34 □	42 □	50 □	58 □	66 □	74 □	82 □	90 □			
C	3 □	11 □	BLANK	19 □	27 □	35 □	43 □	51 □	59 □	67 □	75 □	83 □	91 □		
D	4 □	12 □	20 □	28 □	36 □	44 □	52 □	60 □	68 □	76 □	84 □	92 □			
E	5 □	13 □	21 □	29 □	37 □	45 □	53 □	61 □	69 □	77 □	85 □	93 □			
F	6 □	14 □	22 □	30 □	38 □	46 □	54 □	62 □	70 □	78 □	86 □	94 □			
G	7 □	15 □	23 □	31 □	39 □	47 □	55 □	63 □	71 □	79 □	87 □	95 □			
H	8 □	16 □	24 □	32 □	40 □	48 □	56 □	64 □	72 □	80 □	88 □	96 □	PC		
Sampling Staff: _____												Verifier: _____		Sampling Time: _____	
Blank Lot No: _____												PC Lot No.: _____			
Nucleic Acid Extraction Staff: _____												Verifier: _____		Nucleic Acid Extraction MGISP-960 No.: _____	
MLB (Extraction Reagent) Reagent ID: _____												qPCR Reagent Mix Batch ID: _____			

Print click

Figure 1 COVID-19 Sample Nucleic Acid Test Record.

Print the arranged task excel file 《COVID-19 Sample Nucleic Acid Test Record》, place the print 《COVID-19 Sample Nucleic Acid Test Record》, plate labels and samples together ready for sampling.

9.18. Work Area Preparation

9.18.1. Biosafety cabinet preparation: Turn on UV light for 30min, Push up the front cover to the position of "SASH" and press "FAN" Button. After 3 min, when there is "Di~" sound coming out and the airflow speed reaches 1200m³/h, Biosafety cabinet is ready to use. Fill the 《General Equipment Usage and Maintenance Record》.

9.18.2. Take out Blank Control and Positive Control from Real-time fluorescent RT-PCR kit for detecting 2019-nCoV, Place them in biosafety cabinet for next step.

9.18.3. Print the plate ID labels in quadruplicate each plate ID for a whole day use, plate ID format:

Year-Month-Day-X (For example: 20200213-1, X=0、1、2、3...).



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9.18.4. A Aliquoting:

A aliquoting step process in the biosafety cabinet, prepare the safety cabinet (Mark the plate number information on the front of the deep well plate (20020215-x) according to the task list, and transferring 160µL sample from sample tube to the deep well plate according to the task list number order. When one plate is done, Seal the film.

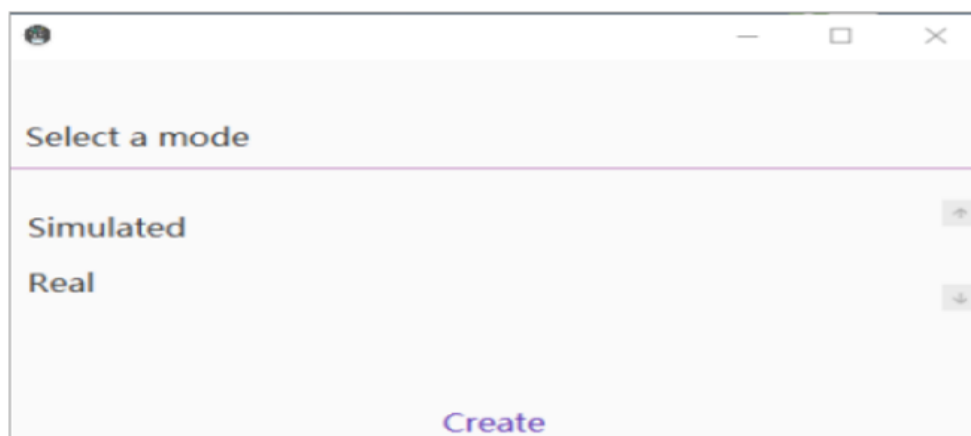
9.19.RNA Extraction:

Refer to MGISP-960 MGI Easy Magnetic Beads Virus DNA/RNA Extraction Kit Instructions.

Full automated system for extraction

9.19.1. MGISP-960 machine Operation

9.19.1.1 Double-click the icon of MGISP-960 on the desktop. The mode selection interface is displayed, as shown in Figure1, Select Real and click Create.





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9.19.1.2 In the Authentication interface, click User Entry to enter the initialization interface.

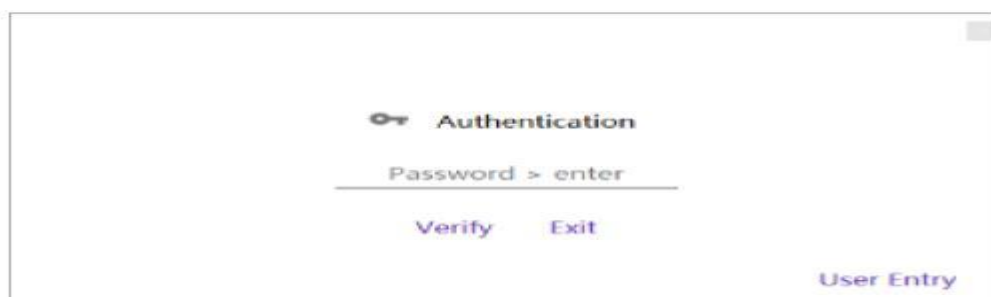
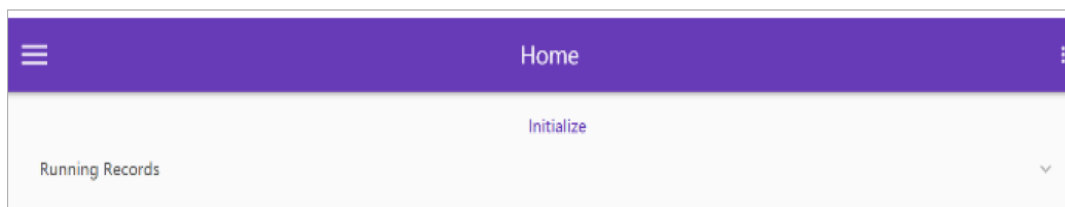


Figure 2. Authentication Interface

9.19.1.3 The initialization interface is displayed, as shown in Figure 3.



9.19.1.4. Click Initialize. The initialization takes about 2 minutes. If “Initialize successfully” is displayed

Note: If the initialization fails, check whether the power switch is turned on, and whether more than one software. program is running. Try to restart the software. If the problem persists, contact MGI technical support

9.19.1.5. Click the menu button and select Run Wizard in the menu.

9.19.1.6. In the Run Wizard interface (Figure 5), click Application, and select [COVID-19]. Click Script and select [JB-A09-023 MGISP-960 Virus DNA RNA Extraction-ONE PLATE] OR [JB-A09-023 MGISP-960 Virus DNA RNA Extraction-TWO PLATE] it depends on your work load choose the program, the machine has two program for running either one plate or two plate. Operation deck arrangement of the first phase is displayed according to program that you choose, as shown in





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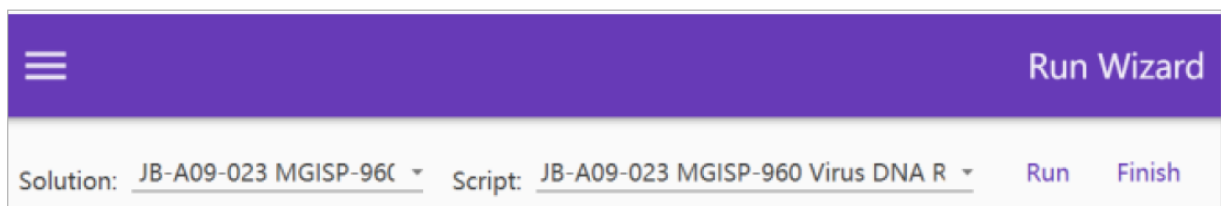
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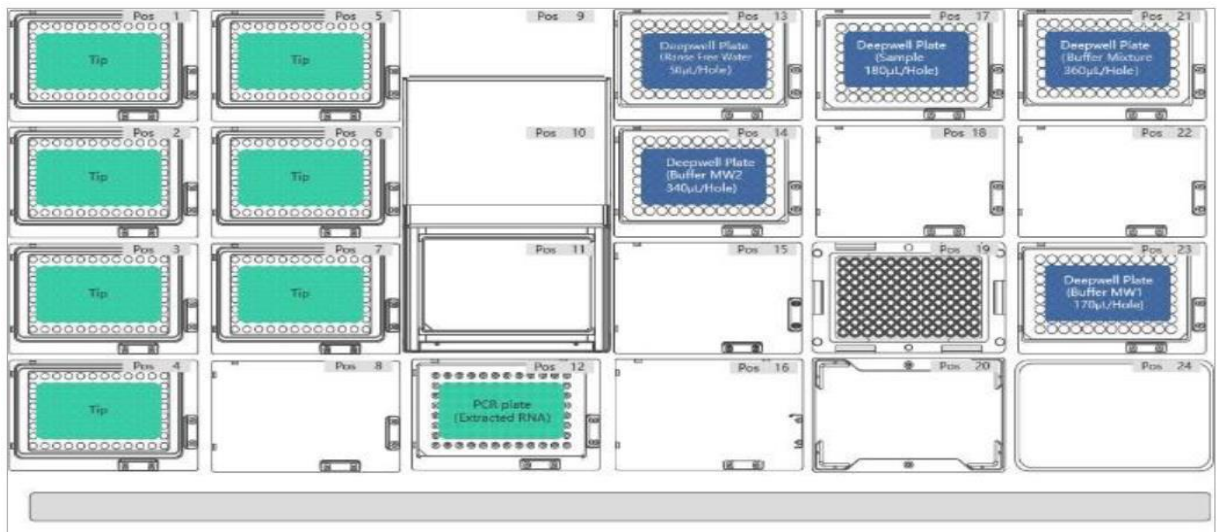
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Figure 6. Follow the on-screen instructions to place the consumables, samples, and reagents, as shown in the Figure 6. Confirm the placement and close the door.



Run Wizard interface (Figure 5)



click run to start.

9.19.1.7. It is expected to run 1h. After the process is finished, the product at Pos12 is taken out. You can pause or resume the workflow if necessary.

9.19.1.8. Dispose of the used deep-well plates, PCR plates, and waste bags to the designated waste area. If all the test for the day is finished, perform a post-clean before powering off the device according to MGISP-960 Cleaning Instructions.





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9.20. Re -Extraction PROCEDURE:

9.20.1. Take the sample out from the freezer and let the sample to thaw and vortex again

9.20.2. Whole plate re-extraction which is happen due to fail of control of the original plate

9.20.3. The work sheet arrangement it will be the same original plate ID+ E for example
(20200501-12 E) which is E referring to Re- Extraction

9.21. INTERFERENCE:

Contamination it will lead to fail of the reading of the negative control, before starting producer make sure you disinfected all items well and safety cabinet

9.22. POTENTIAL SOURCES OF VARIATION:

9.22.1 PERSONAL:

Competent of staff.

9.22.2. MACHINE /EQUIPMENT:

Maintenance

PPM

9.22.3. REAGENT:

Stability of reagent and expiry date

Temperature of refrigerator & freezer

10 CROSS REFERENCE

10.1 Manual operating producer for the machine MGI -960

10.2 MGI Easy Nucleic Acid Extraction Kit User Manual

10.3 kit insert of real time fluorescent

10.4 Real time Fluorescent RT-PCR method sheet insert sheet





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11 RELEVANT DOCUMENTS & RECORDS

- 11.1. COVID-19 Sample Nucleic Acid Test Record
- 11.2. Real-time Fluorescent RT-PCR for Detecting 2019-nCov Quality Control Monitoring Summary Records
- 11.3. Samples storage record
- 11.4. COVID-19 sample disposal record

