Title: Anti-Sars-Cov-2 in Serum and Plasma by Electrochemiluminescence on Roche Cobas 8000 (e801)

PURPOSE

This Standard Operating Procedure (SOP) describes a standard procedure using regulatory requirements for performing Anti-Sars-Cov-2 testing.

SCOPE

This SOP applies to employees in the following divisions and departments or areas:

Global Central Laboratories

(b) (4)

ASSAY INFORMATION

1.0 SARS-CoV-2 is an enveloped, single-stranded RNA virus of the family Coronaviridae, genus Betacoronavirus. All coronaviruses share similarities in the organization and expression of their genome, which encodes 16 nonstructural proteins and the 4 structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N). Viruses of this family are of zoonotic origin. They cause disease with symptoms ranging from those of a mild common cold to more severe ones such as the Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and Coronavirus Disease 2019 (COVID-19). Other coronaviruses known to infect people include 229E, NL63, OC43 and HKU1. The latter are ubiquitous, and infection typically causes common cold or flu-like symptoms. The Elecsys Anti-SARS-CoV-2 assay uses a recombinant protein representing the nucleocapsid (N) antigen for the determination of antibodies against SARS-CoV-2.

External Name	MTM Number	Lab Assay Name	FDA Approval
Anti-Sars-Cov-2	**39339**	**Anti-Sars-Cov-2_39339**	**IVD**

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SAFETY ISSUES

1.0 Standard safety precautions are required for handling laboratory reagents and samples.
2.0 Entry to the laboratory requires appropriate PPE, at a minimum a fully closed lab coat, safety glasses, and gloves. Additional PPE may be required according to department and task performed.
3.0 When handling samples, safety precautions are applied as described in the Bloodborne Pathogen Exposure Plan and Chemical Hygiene Plan.
4.0 The product label is always read before handling reagents and chemicals.
5.0 For more information, the Safety Data Sheet (SDS) can be consulted. SDS information can be found online at www.3eonline.com.
6.0 The PPD Environmental Health and Safety (EHS) representative may be contacted for additional information as needed.

ANALYTICAL PRINCIPLE

1.0 Sandwich principle. Total duration of assay: 18 minutes.
- 1.1.1 1st incubation: 12 µL of sample, biotinylated SARS-CoV-2-specific recombinant antigen and SARS-CoV-2-specific recombinant antigen labeled with a ruthenium complex form a sandwich complex.
- 1.1.2 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- 1.1.3 The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- 1.1.4 Results are determined automatically by the software by comparing the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cutoff value previously obtained by calibration.

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SPECIMEN REQUIREMENTS

Preferred Sample Type(s)		Serum
Alternative Sample Type(s)		Plasma (Lithium heparin, K2EDTA, K3EDTA)
Sample Collection		Blood sample should be collected by venipuncture
Sample Container		Standard separating tube with or without gel
Transport Container		Plastic transport tube
Sample Stability	**Ambient**	(b) (4)
	2-8°C	
	-20°C	
	-70°C	
	F/T Cycles	3
Volume Requirements		Minimum Volume: (b) (4), Preferred Volume: (b) (4)
Special Handling		Not Applicable
Rejection Criteria		Not Applicable
Interfering Substances		Bilirubin: ≤ 1129 µmol/L or ≤ 66 mg/dL Hemoglobin: 1000 mg/dL or 10 g/L Intralipid: 2000 mg/dL Biotin: ≤ 4912 nmol/L or ≤ 1200 ng/mL Rheumatoid factors: 1200 IU/mL IgG: 7.0 g/dL or 70 g/L IgA: 1.6 g/dL or 16 g/L IgM: 1.0 g/dL or 10 g/L

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REAGENTS AND MEDIA

1.0 Reagent Information

Reagent	US Catalog Number	EU Catalog Number	SG Catalog Number	SHA Catalog Number	Vendor
Elecsys Anti-SARS-Cov-2 (e801)	09203079501	09203079190	Not Applicable	Not Applicable	Roche Diagnostics

2.0 Reagent Preparation

Elecsys Anti-SARS-Cov-2	
Preparation	Ready for Use
Storage	2 – 8 º C

CALIBRATION

Calibrator is included with the reagent pack and is not separate.

1.0 Calibration Preparation

Calibrator 1 and 2	
Preparation	Ready for Use
Storage	2 – 8 º C

2.0 Calibration Frequency

2.1 Calibration must be performed once per reagent lot
2.2 After (b) (4) days when using the same reagent lot on the Cobas e801 analyzer
2.3 After 14 days when using the same Cobas e pack on the Cobas e801 analyzer

3.0 Calibration Acceptability

3.1 Calibrators are automatically run in duplicate

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3.2 The Cobas e801 will automatically evaluate the results to determine if they are within 10% and within the parameters specific for that lot

3.3 Please refer to SOP-17669 for proper installation of lot parameters

4.0 Analytical Measurement Range (AMR)

Analytical Measurement Range

US AMR Range	EU AMR Range	SG AMR Range	SHA AMR Range
Assay reported as Negative or Positive	Assay reported as Negative or Positive	Not Applicable	Not Applicable

QUALITY CONTROL AND BATCH ACCEPTANCE CRITERIA

1.0 Quality Control Information

Quality Control	US Catalog Number	EU Catalog Number	SG Catalog Number	SHA Catalog Number	Vendor
(b) (4) Sars-Cov-2	(b) (4)				
(b) (4) Sars-Cov-2					

2.0 Quality Control Preparation

(b) (4) Sars-Cov (Positive)	
Preparation	Ready to Use
Storage	2 – 8 º C

(b) (4) Sars-Cov (Negative)	
Preparation	Ready to Use
Storage	2 – 8 º C

3.0 Quality Control Frequency

3.1 Two levels of quality control must be run before and after running patients.

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3.2 Both levels of quality control must be run directly after calibration.

4.0 Quality Control Acceptability

4.1 Quality Control negative < 1.0
4.2 Quality Control positive > 1.0
4.3 Please refer to SOP-18002
4.4 Refer to SOP-17669 for guidelines and proper installation of lot parameters

EQUIPMENT AND MATERIALS

1.0 Equipment

1.1 Roche Cobas 8000 e801

2.0 Materials

1.1 Elecsys Anti-SARS-Cov-2 (e801)
1.2 (b) (4) Sars-Cov
1.3 (b) (4) Sars-Cov

ASSAY PROCEDURES

GCL Lab Analyst

1.0 Performs daily maintenance
- Refer to SOP-17969 for full detailed instructions

2.0 Activates the Preventative Action check box on the instrument screen
3.0 Removes all reagents with expiration of (b) (4)
4.0 Performs reagent registration once all reagents are loaded
5.0 Orders calibration and QC
6.0 Once calibration and QC is acceptable, loads patient samples into the designated rack for the e801 system

- Refer to SOP-17669 for guidelines and troubleshooting if needed

7.0 Ensures that the samples are bubble-free and the barcodes are clearly visible
8.0 Places the patient rack on the inlet side of the load/unload area
9.0 Presses start twice on the main screen
10.0 For operation details, follows SOP-17969
11.0 For troubleshooting, follows the Cobas e801 user guide

CALCULATIONS AND RESULT REPORTING

1.0 Calculations

Reporting Results	
Reportable Range	Assay reported as Negative or Positive
Repeat Criteria	Not Applicable
Critical Values	Not Applicable
Dilution	Not Applicable
Decimals	Not Applicable
Qualitative Cut-off values	< 1.0 = Negative, > 1.0 = Positive
Maximum Dilution	Not Applicable
Units	Not Applicable
Unit Conversions	Not Applicable

2.0 Result Reporting

Method CV from PI	Achieved CV During Validation
5.4%	100%

REFERENCE RANGES

1.0 Negative

TEST DELAY

1.0 Refer to SOP-17755.

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LIMITATIONS

1.0 SARS-CoV-2 IgG antibodies may be below detectable levels in patients who have been exhibiting symptoms for less than 15 days

2.0 A positive result may not indicate previous SARS-CoV-2 infection. Other information is considered including clinical history and local disease prevalence, in assessing the need for a second but different serology test to confirm an immune response.

3.0 A negative test result does not rule out the possibility of an infection with SARS-CoV-2. Serum or plasma samples from the early (pre-seroconversion) phase of illness can yield negative findings. Therefore, this test cannot be used to diagnose an acute infection. Also, over time, titers may decline and eventually become negative.

DEFINITIONS

None

REFERENCES

SOP-17755 (Legacy Number GCL-LAB-0199) Guidelines for the Communication of Assay Issues to Sponsors, Clinical Teams and Investigators

SOP-18002 (Legacy Number GCL-LAB-0172) Quality Control (Internal) Testing and Review

SOP-17669 (Legacy Number GCL-LAB-0699) Roche 6000/8000 Calibration and Quality Control Guidelines

SOP-17969 (Legacy Number GCL-LAB-0816) Roche Cobas 8000 Operation Maintenance

VR-GCL-EU-2020-10-590; Anti-Sars-Cov-2 in Serum and Plasma by Electrochemilumiluminescence on Roche Cobas (e801) Primary Validation Summary, Issue Date, 20Oct2020

Package Insert; Elecsys Anti-SARS-CoV-S Cobas, V 6.0, 2021-02

Package Insert; (b) (4) SARS-CoV (b) (4)

Package Insert; (b) (4) SARS-CoV (b) (4)

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REVISION SUMMARY

Not Applicable

REVISION HISTORY

Version	Action	Effective Date
SOP-18550 1.0	*New document*	*28 Apr 2021*

Document Approvals

Approved Date: 14 Apr 2021

Task: Approvers Approval Verdict: Approve changes & release	Basel Kashlan, Sr Dir Labs (Basel.Kashlan@ppdi.com) Business Approver 14-Apr-2021 13:39:48 GMT+0000

Task: QA Approval Verdict: Approve changes & release	(b) (6) (b) (6) @ppdi.com) Quality Approval 15-Apr-2021 02:00:37 GMT+0000