SARS-CoV-2 IgG Calibration Verification / Linearity Test Kit

INTENDED USE
VALIDATE SARS-CoV-2 IgG Calibration Verification / Linearity Test Kit solutions are intended for *in vitro* diagnostic use in the quantitative determination of linearity, calibration verification and verification of reportable range in automated instrument systems for the following analytes: SARS-CoV-2 IgG (COV IgG)

Each test kit consists of one bottle each of Levels 1 through 6. Each bottle contains 3.0 milliliters. There exists a linear relationship among Levels 1 through 6 for each set.

Note: Level 6 is intended for Abbott Architect/Alinity and the Beckman Coulter DxI.

SUMMARY
For each VALIDATE Calibration Verification / Linearity Test Kit, multiple levels are provided to establish the relationship between theoretical and actual performance of each of the included analytes. The VALIDATE Calibration Verification / Linearity Test Kit will assist in the documentation of linearity, calibration verification and verification of linear range required by many inspection agencies. The solutions will also provide assistance when troubleshooting instrument systems, reagent problems and calibration anomalies.

REAGENTS
Reactive Ingredients:
Purified chemicals and constituents of human and/or animal source in human plasma.

VALIDATE SARS-CoV-2 is manufactured using LGC The Native Antigen Company's Human IgG1 Anti-SARS-CoV-2 Spike (S1) RBD Antibody (DH6) which is a recombinant humanized monoclonal antibody against SARS-CoV-2 receptor binding domain (RBD) protein. This antibody is neutralizing against SARS-CoV-2, but not against SARS-CoV-1 or MERS-CoV.

The Native Antigen Company's SARS-CoV-2 monoclonal antibody was characterized using a Q-Exactive Plus Orbitrap to check for product integrity and purity. Epitope mapping was carried out by hydrogen deuterium exchange mass spectrometry (HDX-MS) using a Synapt G2Si coupled with a LEAP PAL system. The intact protein analysis of the original glycosylated SARs-CoV-2 monoclonal antibody showed five different glycan species with G0F/G0F (149,154 Da) as the most abundant form. The HDX-MS results report the most significant antigenic binding epitope as amino acids 418-437 within the receptor binding domain (RBD), Spike protein 1

Nonreactive Ingredients:
Preservatives and stabilizers.

Precautions and Warnings:
For In Vitro Diagnostic Use
Disposal of all waste material should be in accordance with local guidelines.

WARNING: Potentially Biohazardous
Human source material is considered potentially biohazardous. Use the Centers for Disease Control (CDC) recommended universal precautions for handling VALIDATE products.

STORAGE AND STABILITY
The **VALIDATE** SARS-CoV-2 IgG Calibration Verification / Linearity Test Kit is stored at -10° to -25°C. ***Do NOT store in a frost-free freezer.*** Test kits are stable until the expiration date printed on the bottle and storage container when handled according to instructions***. A maximum of four (4) freeze-thaw cycles is recommended.***

PREPARATION
Prior to use, remove the **VALIDATE** SARS-CoV-2 IgG Calibration Verification / Linearity Test Kit from storage and allow to come to room temperature (18° to 25°C). Invert gently several times before dispensing.

To maximize stability, it is recommended that exposure to room temperature be minimized. Tightly cap opened bottles and return to -10° to -25°C immediately after dispensing.

Discard any solutions that appear to have gross bacterial contamination.

VALIDATE Calibration Verification / Linearity Test Kits should be treated in the same manner as patient samples. If dilutions or pre-treatment are required as part of the testing procedure, follow the manufacturer's instructions.

ASSAY
Analyze each level in replicates. If following the CLSI EP6 guidelines for linearity, use a random analytical sequence to assay each level.

CALCULATION OF RESULTS
VALIDATE Calibration Verification / Linearity material is prepared in a manner such that an equal distance (delta) exists between Levels 1 through 5. This dilution scheme is consistent with the CLSI EP6 recommendation for preparing linearity sets.

Level 6 is manufactured based on a known relationship to Levels 1 and 5. The theoretical value is determined by multiplying the Delta value by the factor provided: 82.79

Two examples for calculating the theoretical values of Levels 1 through 6 are provided below.

Example 1:
Choose two consecutive levels and calculate the delta between the recovered values. The following example demonstrates the use of the delta between Levels 2 and 3 to calculate the theoretical value for Levels 1, 4, 5 and 6.

Level 3 Recovered – Level 2 Recovered = Delta

Level 1 Theoretical = Level 2 Recovered – Delta
Level 4 Theoretical = Level 3 Recovered + Delta
Level 5 Theoretical = Level 4 Theoretical + Delta
Level 6 Theoretical = Delta * 82.79

NOTE: The user can select the calculated delta between any two consecutive levels to calculate the theoretical values. Typically, the user should choose an area of recovery known to be linear for the method being studied.

Example 2:
Theoretical values can be determined using the recovered values for Levels 1 and 5. Using this method, the following formulas apply:

Level 2 Theoretical = 0.75 * (Level 1) + 0.25 * (Level 5)
Level 3 Theoretical = 0.5 * (Level 1) + 0.5 * (Level 5)
Level 4 Theoretical = 0.25 * (Level 1) + 0.75 * (Level 5)
Level 6 Theoretical = Delta * 82.79

(Level 3 Theoretical – Level 2 Theoretical = Delta)

After theoretical values are calculated, for each analyte plot the expected (Theoretical) value on the x-axis versus the Recovered value on the y-axis using standard linear graph paper. If the system is linear, the plot should approximate a straight line. The point at which the line is no longer straight can be used to determine the limit of linearity or the reportable range.

Data reduction is available from LGC Clinical Diagnostics. Commercially available linear regression software may also be used. The software should provide data point display and x-y graphical presentation. Linear regression should be interpreted using standard statistical analysis and the results should be compared with the instrument manufacturer's claims for linearity or with individual laboratory performance requirements. The degree of acceptable nonlinearity is an individual judgment based on methodology, clinical significance and medical decision levels of the test analyte.

LIMITATIONS
VALIDATE Calibration Verification / Linearity Test Kit solutions are not intended for use as routine quality control materials or as

calibration materials.

EXPECTED VALUES

VALIDATE Calibration Verification / Linearity Test Kits are manufactured such that an equal distance (delta) exists between levels as recommended by CLSI EP6 for assessing linearity. As the distance between Levels 1 through 5 is equal, any two levels between 1 and 5 can be held to be 'true' when assayed and the theoretical values for each of the other three levels can be calculated allowing this test kit to be used on multiple automated instrument systems. The theoretical value for Level 6 is calculated based on a known relationship to Levels 1 and 5 and can be calculated using the factor for each analyte listed in the factor table provided in the **CALCULATIONS OF RESULTS** section of this insert.

The reagent manufacturer's recommended diluent can be used to make dilutions of the low level to obtain a result lower than that level, if needed.

TYPICAL VALUES

Actual results obtained may vary depending on instrumentation, methodology and assay temperature. Results may also be dependent on the accuracy of the instrument / reagent system calibration. The degree of acceptable nonlinearity is an individual judgment based on methodology, clinical significance and medical decision levels of the test analyte.

Typical recovered values are calculated based on CLSI EP6 equal distance (delta) manufacturing protocols where two recovered values can be held as "True", and other levels calculated based on equal distance. **VALIDATE** typically uses Level 1 and Level 3 to calculate additional target values.

Adaptation of the standard additions method developed by the National Measurement Laboratory at LGC (Pang and Cowen, 2017 - DOI: 10.1038/s41598-017-17823-y) for use with immunoassays has enabled the quantitation of exogenous analyte concentrations within serological test samples. The method accommodates the non-linear correlation between the total concentration of the analyte (calibrant and exogenous analyte) and the immunoassay signal output. The method has been implemented to quantitate the concentration of IgG within VALIDATE SARS-CoV-2 IgG by replicate immunoassays of Level 5 (n=3) from which the concentrations of the other standards have been derived from these actual data.

Batch: 10685125

Analyte	Units	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
SARs-CoV-2 IgG	µg/mL	0	0.34	0.67	1.01	1.34	27.4

CE Symbols – This product fulfills the requirements of the European Directive 98/79/EC for *in vitro* medical devices. The following symbols may be used where applicable in labeling for LGC Clinical Diagnostics products:

LOT	**Lot Number**
	Expiration Date
	Manufacturer
	Storage Temperature
IVD	***In Vitro Diagnostic Medical Device***
REF	**Catalog Number**
	Insert
	Biological Risk
2	**Do Not Reuse**

CE EC REP MEDIMARK® Europe |11, rue Émile Zola BP 2332
38033 Grenoble Cedex 2 – France | www.medimark-europe.com

For a list of countries for which VALIDATE® is CE marked and available for purchase, see:
http://www.mainestandards.com/Products/ce_reg.php

Rx Only

ORDERING INFORMATION

ORDER NO.: 510mm

VALIDATE SARS-CoV-2 IgG
Calibration Verification / Linearity Test Kit:
Set 1: 6 x 3 mL

CONTACT INFORMATION:

LGC Clinical Diagnostics, LLC.
221 US Route 1
Cumberland Foreside, ME 04110 USA

1-800-377-9684
+1-207-892-1300
+1-207-892-2266 Fax
msc.sales@LGCGroup.com
msc.techsupport@LGCGroup.com
www.mainestandards.com