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Novel neutralizing anti-S1 SARS-CoV-2 human monoclonal antibody formulation for use as a cross-platform EQA sample and prospective quality controls

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MICROBIX

INTRODUCTION

Serological tests are a valuable diagnostic methodology for evaluating SARS-CoV-2 post-infection immunity. Specifically, they are a useful tool for monitoring the seroconversion associated with convalescence or vaccination and can help identify the possible need for re-vaccination within a given timeframe.

Currently used convalescent patient plasma pools and humanized mouse monoclonal antibody formulations are not reliable for use as Quality Control (QC) or External Quality Assessment (EQA) samples, due to their poor repeatability, cross-reactivity, and lack of linearity. There is a pressing need for reliable QC and EQA materials that cover the diverse SARS-CoV-2 Serological IVD ecosystem.

AIM

To develop and demonstrate the performance of anti-S1 human monoclonal antibody formulated in a plasma-like matrix. The material has been benchmarked against the WHO reference material (NIBSC code:20/136), permitting the standardization of various serological assays and systems. The formulation is non-infectious, non-cross-reactive, and highly repeatable.

MATERIALS & METHODS

Microbix's panel of serological samples is comprised of seven different levels of neutralizing anti-S1 SARS-CoV-2 human monoclonal antibody (hMAb) in a proprietary human plasma-like matrix. The performance of the anti-S1 SARS-CoV-2 hMAb levels was evaluated using the Anti-SARS-CoV-2 QuantiVac ELISA (IgG) (Euroimmun) benchmarked against the NIBSC code:20/136 standard and the Elecsys ACOV2 / ACOV2 S (Roche) (Table 1 and 2). Three levels representing high (H), medium (M) and low (L) levels were selected for additional feasibility studies by clinical laboratories (1WA, OASYS Table. 3) and were confirmed internally by serological rapid test POCT detection methodologies.

Product Name	Cat#	Level
PROCEEDx™ anti-SARS-CoV-2 Ab Positive Sample L1	VP-19-19L1	H
PROCEEDx™ anti-SARS-CoV-2 Ab Positive Sample L2	VP-19-19L2	H
PROCEEDx™ anti-SARS-CoV-2 Ab Positive Sample L3	**VP-19-19L3**	**H**
PROCEEDx™ anti-SARS-CoV-2 Ab Positive Sample L4	VP-19-19L4	M
PROCEEDx™ anti-SARS-CoV-2 Ab Positive Sample L5	**VP-19-19L5**	**M**
PROCEEDx™ anti-SARS-CoV-2 Ab Positive Sample L6	VP-19-19L6	L
PROCEEDx™ anti-SARS-CoV-2 Ab Positive Sample L7	**VP-19-19L7**	**L**

Table 1. Samples used for OEM and internal feasibility studies

EQA Product Name	Cat#	Level
anti-SARS-CoV-2 Ab Positive Sample L3	PT-19-19L3	H
anti-SARS-CoV-2 Ab Positive Sample L5	VP-19-19L5	M
anti-SARS-CoV-2 Ab Positive Sample L7	VP-19-19L7	L

Table 2. Samples used for EQA pilot programs

PROCEED PT

RESULTS

1. *Data from OEMs – Semiquantitative Tests*

A. Euroimmun - Anti-SARS-CoV-2 QuantiVac ELISA (IgG) [1]

2606-10 G ~ E201201AO ~ 17.12.2020

No.	Sample	Volume in mL Original	IgG Result 1 RU/ mL	IgG Result 2 RU/ mL	IgG Mean RU/ mL	IgG Mean BAU/ mL
			Pos: ≥ 11	**Pos: ≥ 11**	**Pos: ≥ 11**	**Converted [1]**
			bl: 8 - <11	bl: 8 - <11	bl: 8 - <11	
1	171220-L1	2*1,5	>120	>120	>120	>384 (MR)
2	171220-L2	2*1,5	55.3	57.2	56.3	180.16
3	**171220-L3**	2*1,5	27.8	27.2	27.5	88.00
4	171220-L4	2*1,5	15.9	14.6	15.3	48.96
5	**171220-L5**	2*1,5	7.8	7.5	7.6	24.32
6	171220-L6	2*1,5	4.2	4.2	4.2	13.44
7	**171220-L7**	2*1,5	2	1.9	2	6.40
8	Blank	2*1,5	>1	>1	>1	>3.2

Table 1. Results with interpretation - Euroimmun

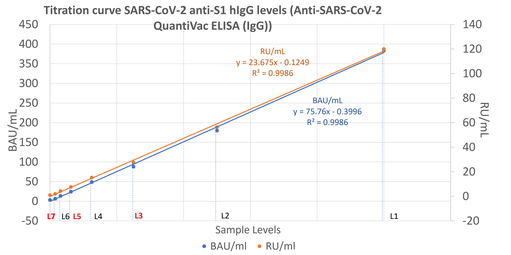


Fig 1. Results with interpretation - Euroimmun

B. Roche - Elecsys® Anti-SARS-CoV-2

SARS-CoV-2 Anti S1 IgG in 1.5 mL Vial		
Instrument	**e411**	**e411**
Assay	**Elecsys® ACOV2**	**Elecsys® ACOV2 S**
Interpretation		
Non-Reactive	COI < 1.0	<0.800 BAU/ mL
Reactive	COI ≥ 1.0	≥ 0.800 BAU/ mL

Sample	COI	Result	Concentration [BAU/ mL]	Result	Interpretation
Lot 171220-L1	0.24	Non-Reactive	>MR	>250 BAU/ mL	Reactive
Lot 171220-L2	0.24	Non-Reactive	>MR	>250 BAU/ mL	Reactive
Lot 171220-L3	**0.238**	**Non-Reactive**	**>MR**	**>250 BAU/ mL**	**Reactive**
Lot 171220-L4	0.246	Non-Reactive	192	192 BAU/ mL	Reactive
Lot 171220-L5	**0.239**	**Non-Reactive**	**108**	**108 BAU/ mL**	**Reactive**
Lot 171220-L6	0.246	Non-Reactive	58.1	58.1 BAU/ mL	Reactive
Lot 171220-L7	**0.261**	**Non-Reactive**	**31**	**31.0 BAU/ mL**	**Reactive**

Table 2. Results with interpretation - Roche

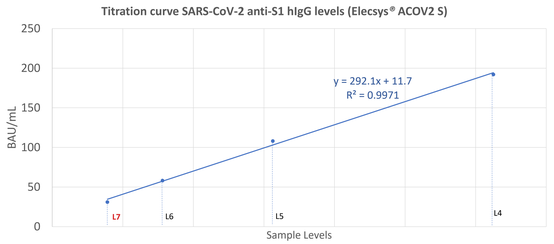
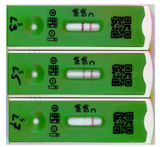


Fig 2. Results with interpretation - Roche

2. *Internal Data from POCT BTNX Rapid Response COVID IgG/IgM*



REACTIVE (++++)

REACTIVE (++)

REACTIVE (+)

Legend
++++= High Positive
++ = Medium Positive
+ = Low Positive

Fig 3. Results with interpretation - BTNX

3. *Data from Oneworld Accuracy EQA Pilot - OASYS informatics system*

A. Platforms with confirmed performance (combined) by EQA samples

Tests Used By Participants in Anti-S1 SARS-CoV-2 IgG Pilot Study		
Manufacturer	Name of test	Number of Users
Abbott	SARS-CoV-2 IgG (N-protein)	1
GenScript	cPass™ SARS-CoV-2 Neutralization Antibody Detection Kit[2]	1
BTNX	Rapid Response COVID IgG/IgM	1

B. Statistical data Oneworld Accuracy (1WA OASYS pilot study 2021)

Summary of Anti-S1 SARS-CoV-2 IgG Pilot Study S-protein based tests - detectability

2 Participants / 2 Countries	18 Number of Responses / 2 Participating Assays	100% Success Rate for H Sample (L3)	100% Success Rate for M Sample (L5)	50% Success Rate for L Sample (L7)

Summary of Anti-S1 SARS-CoV-2 IgG Pilot Study N-protein based test – specificity

1 Participant / 1 Country	9 Number of Responses / 1 Participating Assay	100% Success Rate for H Sample (L3)	100% Success Rate for M Sample (L5)	100% Success Rate for L Sample (L7)

[2] GenScript cPass™ SARS-CoV-2 Neutralization Antibody Detection Kit is a blocking immunoassay designed for qualitative direct detection of total neutralizing antibodies to SARS-CoV-2 in human serum and K2-EDTA plasma. The assay is designed to detect protecting levels of neutralizing antibodies. Negative result refers to < 30% Signal Inhibition and therefore low level of neutralizing antibodies will be considered negative result.

CONCLUSIONS

The novel anti-S1 SARS-CoV-2 hMAb formulations showed excellent linearity when evaluated with the Anti-SARS-CoV-2 QuantiVac ELISA (IgG) and Elecsys ACOV2. Additionally, their successful detection across testing platforms and methodologies demonstrates that these formulations are cross-platform compatible and have the potential to be used for benchmarking the performance of current tests. Although, notably, the numerical BAU/mL values differed between assays, which can be explained by differences in the use of antigens and applied testing methods. Lastly, the anti-S1 SARS-CoV-2 hMAb formulations can be used as prospective cross-platform EQA samples and quality controls for emerging SARS-CoV-2 IgG quantification tests designed to monitor vaccination efficacy.

REFERENCES

1. Anti-SARS-CoV-2 QuantiVac ELISA (IgG) (Euroimmun) Technical bulletin; EI_2606_D_UK_E.pdf
2. GenScript cPass™ SARS-CoV-2 Neutralization Antibody Detection Kit Instruction for Use

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