Supplementary Material

COVID-19 Antibody Detecting Rapid Diagnostic Tests Show High Cross-Reactivity When Challenged with Pre-Pandemic Malaria, Schistosomiasis and Dengue Samples

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Supplementary Table S1. Extra information of different COVID-19 antibody detecting products and EIA according to manufacturer, Instructions for Use and product regulation. Data are those obtained at selection and procurement (August-September 2020). Unless otherwise stated, data are those from the Instructions for Use or the labeling of the product. Wantai RDT product has a single test line, no information was given about the nature of the antibody detected (ND = no data). Claimed specimen: S = serum, P = plasma, WB = whole blood. Sensitivity and specificity results according to FIND independent SARS-CoV-2 Ab evaluations are found on https://www.finddx.org/sarscov2-eval-antibody/ (NA = not applicable). Products with "*" had no detecting antigen mentioned in the instructions for use, information was retrieved from the manufacturer or the FDA EUA or WHO EUL, unless otherwise stated (column antigen used for detection). Abbreviations: EIA = enzyme immunoassay, CE = Conformité Européenne (CE Mark), FDA EUA = U.S. Food and Drug Administration Emergency Use Authorization, WHO EUL = World Health Organization Emergency Use Listing, FAGG = Federal Agency for Medicines and Health Products, FIND = Foundation for Innovative New Diagnostics, IFU = Instructions for Use. Products with "**" did not mention the use of fingerstick blood as a possible specimen. Cellex recommend not to use fingerstick specimens, as it is not validated. Information about regulatory status was obtained during the procurement of the RDT products in August 2020. Products with "ǂ" mentioned in the instructions for use not to use frozen whole blood to perform RDT testing.

Product	Manufacturer	City (Country)	Antigen used for detection	IgG/IgM	Claimed specimen	Claimed sensitivity	Claimed specificity	Product code	Lot number	Shelf life upon reception (months)	IFU version	Date IFU	Price/test (in euros, taxes not included)	Regulatory authorization (CE, FDA, FAGG)	Listed on WHO EUL	FIND	Results FIND sensitivity	Results FIND specificity
Wantai SARS-CoV-2 Ab Rapid Test	Wantai Bio-Pharm	Beijing (China)	S *	ND	S/P/WB ǂ	99,7%	98,9%	WJ-2750	JNB20200304	6	20/04	26/04/2020	5,90	CE, FDA	Yes	Yes	Pending Finalization	
COVID-19 IgG/IgM Rapid Test Cassette	Healgen	Houston (USA)	S *	IgG/IgM	S/P/WB ǂ	IgG:97,2% IgM: 87,9%	IgG:100% IgM: 100%	GCCCOV-402a	2003309	17	B21854-02	4/03/2020	11,25	CE	No	No	NA	NA
TODA CORNODIAG +	Todapharma	Strasbourg (France)	N *	IgG/IgM	S/P/WB	IgG:100% IgM:100%	IgG:100% IgM:100%	2275+/25	2005081A	19	Version 3	03/08/2020	9,45	CE	No	No	NA	NA
Rapid 2019-nCOV IgG/IgM Combo Test Card	Boson Biotech	Fujian (China)	N *	IgG/IgM	S/P/WB **	87,8%	99,0%	1N38C2	20031926	11	81985	20/03/2020	8,75	CE	No	Yes	NA	NA

SARS-CoV-2 IgM/IgG Antibody Test Kit	Biohit	Hefei (China)	N *	IgG/IgM	S/P/WB	IgG:97,5% IgM: 97,5%	IgG:100% IgM: 99,5%	NA	SA200401	6	Version02	22/02/2020	2,55	no CE, FDA	Yes	Yes	NA	NA
PanBio COVID-19 IgG/IgM Rapid test device	Abbott	Jena (Germany)	N *	IgG/IgM	S/P/WB [1]	97,8%	92,8%	ICO-T402	COV0052023	7	NA	6/06/2020	6,00	CE, FAGG	No	No	Withdrawn	
QuickZen COVID-19 IgM/IgG	ZenTech	Angleur (Belgium)	RBD	IgG/IgM	S/P/WB [1]	IgG:100% IgM:97%	IgG:97% IgM:99,1%	SLW-25	SLW25-007A	18	S-LW-MZ-002	1/04/2020	9,80	no CE, FAGG	No	Yes	55.1%	99.0%
StrongStep SARS-CoV-2 IgM/IgG Antibody Rapid Test	Liming Bio	Jiangsu (China)	N + S *	IgG/IgM	S/P/WB ** [1]	IgG:93,3% IgM: 98,7%	IgG:98,7% IgM: 100%	502090	2006003	19	V4.0	30/05/2020	2,55	no CE, FAGG	No	Yes	NA	NA
2019-nCOV IgG/IgM Rapid Test	Dynamiker	Tianjin (China)	N + S	IgG/IgM	S/P/WB	93,2%	95,3%	DNK-1419-1	200501	12	NA	NA	11,00	CE, FAGG	No	Yes	69.7%	95.3%
qSARS-COV-2 IgG/IgM Rapid Test	Cellex	North Carolina (USA)	N + S *	IgG/IgM	S/P/WB **	93,8%	96%	5515C025	20210	9	NA	NA	17,00	CE	No	Yes	Withdrawn	
COVID-19 IgG/IgM Rapid Test Cassette	SureScreen Diagnostics	Derby (UK)	N + RBD *	IgG/IgM	S/P/WB [1]	IgG:100% IgM: 91,8%	IgG:99,5% IgM: 99,2%	COVID19C	COV20040037	17	RP327102	5/03/2020	7,36	CE, FAGG	No	No	NA	NA
COVID-19 IgG/IgM Detection Kit (Colloidal Gold)	Singuway	Shenzhen (China)	N + RBD *	IgG/IgM	S/P/WB **	≥95-100%	100%	NA	200404A	no expiry date	402-000032-00V1.2en	28/03/2020	9,50	no CE	No	No	NA	NA
COVID-19 IgM/IgG Ab Test Cassette	Multi-G	Antwerpen (Belgium)	N + RBD + S *	IgG/IgM	S/P/WB ** [1]	IgG:93% IgM: 82%	IgG:96% IgM: 97,5%	MGS	COV1252006A	8	Rev01 20200623	23/06/2020	5,00	CE	No	Yes	NA	NA

2019 nCOV IgG SPIKE EIA	Launch Diagnostics Limited/DiaPro IgG EIA	Milano (Italy)	S	IgG	S/P [1]	100%	>98%	COV19Gspike.CE/S	0720	12	rev. 0c	1/06/2020	350,00	CE	No	No	NA	NA
2019 nCOV IgM EIA	Launch Diagnostics Limited/DiaPro IgM EIA	Milano (Italy)	N + S	IgM	S/P [1]	98%	98%	COV19M.CE.192/S	0420/2AA	9	rev. 2c	1/06/2020	840,00	CE	No	No	NA	NA

Supplementary Table S2. Classification of Country of Travel or Residence per disease, traveler type and gender.
Countries are classified according to the United Nations Statistics Division for Geographic Origins (unstats.un.org/unsd/methodology/m49/).
Abbreviations: VFR = visiting friends & relatives.

Country of Travel or Residence				Disease (samples)				Traveler Type (patients)			Gender (patients)	
				Malaria (*n* = 153)	Dengue (*n* = 20)	Schistosomiasis (*n* = 23)	Total disease (*n* = 196)	Expatriates & Travelers (*n* = 51)	VFR & migrants (*n* = 66)	No data (*n* = 79)	Male (*n* = 124)	Female (*n* = 72)
Africa	Northern Africa		Morocco	1	-	-	1	-	-	1	1	-
			Sudan	1	-	1	2	1	1	-	2	-
			Total	2	-	1	3	1	1	1	3	-
	Sub-Saharan Africa	Eastern Africa	Burundi	1	-	2	3	2	-	1	-	3
			Eritrea	1	-	1	2		2	-	2	-
			Ethiopia	3	-	1	4	1	3	-	3	1
			Kenya	1		-	1	-	-	1	-	1
			Madagascar	1	-	-	1	1	-	-	1	-
			Malawi	1	-	-	1	1	-	-	1	-
			Mozambique	1	-	-	1	-	-	1	1	-
			Rwanda	2	-	6	8	6	2	-	4	4
			Somalia	-	1	-	1	1	-	-	1	-
			Uganda	3	-	-	3	1	2	-	1	2
			United Republic of Tanzania	1	-	-	1	1	-	-	1	-
			Total	15	1	10	26	14	9	3	15	11

Africa	Sub-Saharan Africa	Middle Africa	Angola	1	1	1	3	1	2	-	2	1
			Cameroon	16	-	-	16	-	5	11	10	6
			Central African Republic	1	-	-	1	1	-	-	1	-
			Chad	2		-	2	2	-	-	1	1
			Congo	-	1	-	1	-	1	-	1	-
			Democratic Republic of the Congo	28	-	-	28	8	12	8	17	11
			Gabon	1	-	1	2	-	-	2	-	2
			Total	49	2	2	53	12	20	21	32	21
		Western Africa	Benin	2	-	-	2	1	-	1	2	-
			Burkina Faso	6	-	-	6	1	2	3	4	2
			Côte d'Ivoire	5	1	-	6	2	2	2	4	2
			Ghana	16	-	4	20	6	5	9	11	9
			Guinea	10	-	2	12	-	8	4	9	3
			Liberia	3	-	1	4	-	4	-	2	2
			Mali	2		1	3	-	1	2	2	1
			Nigeria	7	-	-	7	-	7	-	5	2
			Senegal	5	1	1	7	1	1	5	5	2
			Sierra Leone	2	-	-	2	-	-	2	1	1
			Togo	3	-	-	3	-	2	1	2	1
			Total	61	2	9	72	11	32	29	47	25

Americas	Latin America and Caribbean	Caribbean	Cuba	-	1	-	1	1	-	-	-	1
			Haiti	-	2	-	2	1	1	-	1	1
		Central America	Mexico	-	1	-	1	1	-	-	-	1
			Nicaragua	-	1	-	1	1	-	-	-	1
		South America	Ecuador	-	1	-	1	-	-	1	-	1
			Suriname	-	1		1	1	-	-	1	-
		Total		0	7	0	7	5	1	1	2	5
Asia	South-eastern Asia		Cambodia	1	1	-	2	-	-	2	1	1
			Indonesia	-	1	-	1	1	-	-	1	-
			Lao People's Democratic Republic	-	-	1	1	1	-	-	-	1
			Philippines	-	1	-	1	1	-	-	1	-
			Thailand	-	2	-	2	1	-	1	2	-
	Southern Asia		India	6	2	-	8	3	-	5	6	2
			Pakistan	1	-	-	1	-	-	1	1	-
			Sri Lanka	-	1	-	1	-	1	-	1	-
	Total			8	8	1	17	7	1	9	13	4
No data				17	-	-	17	1	2	14	11	6

Supplementary Table S3. Pilot testing of the control samples and the invalid test rates per RDT product.

For Cellex RDT product, only 158 samples were tested; for the DiaPro IgG & IgM EIA product, 94 serum and 17 plasma samples were tested.

Pilot testing: commercial controls were Multichem ID-COVID19G/M control and Multichem ID-COVID19 Neg (ZenTech, Angleur, Belgium). Result (pos/neg) and ratio are given for the patient control and commercial controls tested with DiaPro IgG and IgM EIA. Positive serum patient control was confirmed by in-house SARS-CoV-2 virus neutralization, negative serum patient control was a healthy person tested negative by WANTAI SARS-CoV-2 Ab ELISA (Wantai, Beijing, China). Abbreviations: EIA = enzyme immunoassay Results for IgG and IgM lines are presented as negative (N) and by line intensity: very faint (VF), faint (F), weak (W), medium (M) and strong (S). Invalid testing: types of invalid test results include: red background obscuring the test line (ORB), incomplete migration (MI), no control line visible (NCL), failed migration (FM), patchy broken test line (PL) and strip misplaced in cassette (SM) according to WHO round testing 2018 (https://www.who.int/malaria/publications/atoz/9789241514965/en/).

Product	Number of samples tested	Number of cross-reactions	Pilot testing control samples								Numbers (%) of invalid test results	Type of invalid test result (numbers)					
			Negative patient control		Positive Patient control		Multichem negative control		Multichem positive control			ORB	MI	NCL	FM	PL	SM
Wantai	220	85	N		M		N		W		1 (0.5%)	-	-	-	-	1	-
Healgen	219	67	N	N	F	S	N	N	S	W	2 (0.9%)	2	-	-	-	-	-
Toda	220	10	N	N	F	VF	N	N	F	VF	0	-	-	-	-	-	-
Boson	219	116	N	N	M	F	VF	N	M	VF	3 (1.4%)	-	-	-	-	3	-
Biohit	220	34	N	N	W	W	N	N	F	VF	0	-	-	-	-	-	-
Panbio	220	39	N	N	M	N	N	N	W	N	0	-	-	-	-	-	-
QuickZen	220	24	N	N	VF	M	N	N	VF	VF	42 (19.1%)	39	1	-	-	2	-
StrongStep	217	13	N	N	W	W	N	N	N	N	0	-	-	-	-	-	-
Dynamiker	220	73	N	VF	W	W	VF	VF	W	W	8 (3.6%)	5	1	-	-	-	2
Cellex	158	7	N	N	M	W	N	N	W	N	7 (4.4%)	-	-	7	-	-	-
SureScreen	220	12	N	N	W	M	N	N	S	VF	5 (2.3%)	5	-	-	-	-	-
Singuway	220	44	N	N	N	M	N	N	F	F	0	-	-	-	-	-	-
Multi-G	220	12	N	N	W	VF	N	N	W	N	4 (1.8%)	3	-	-	-	25	-
DiaPro IgG EIA	111	2	neg (0.7)	-	pos (3.2)	-	neg (0.74)	-	pos (5.99)	-	NA	-	-	-	-	-	-
DiaPro IgM EIA	111	18	-	neg (0.5)	-	pos (1.1)	-	pos (3.16)	-	pos (4.74)	NA	-	-	-	-	-	-

Total samples	3015	556	-	-	-	-	-	-	-	-	72 (2.4%)	54 (75.0%)	2 (2.8%)	7 (9.7%)	-	31 (43.1%)	2 (2.8%)
Total serum samples	1390	267	-	-	-	-	-	-	-	-	1 (0.07%)	-	1 (100%)	-	-	-	-
Total whole blood samples	1625	270	-	-	-	-	-	-	-	-	71 (4.4%)	54 (76.1%)	1 (1.4%)	7 (9.9%)	-	31 (43.7%)	2 (2.8%)

Supplementary Table S4. Cross-reactions according to the test lines affected and test line intensities for the different RDT products.

Data of test line reactivity are those obtained by consensus reading; data about line-intensity are those scored by observer 1. All data are %, unless otherwise stated. Invalid results are subtracted. Proportions of cross-reactions for Wantai were given as total Ig, proportions of intensities of cross-reactive lines were very faint (96.5%, faint (2.4%) and medium (1.2%) (mentioned with "*")). Abbreviations: NA = not applicable.

Product	Detecting antigen	Test lines affected					Line intensity (read by observer 1)											
							IgG						IgM					
		Nr of cross-reactions	IgG only	IgM only	Total Ig	IgG+IgM	*Nr of cross-reactive lines*	very faint	Faint	Weak	Medium	Strong	*Nr of cross-reactive lines*	Very faint	Faint	Weak	Medium	Strong
Toda	N	*10*	10.0	60.0	NA	30.0	*4*	25.0	25.0	50.0	-	-	*6*	66.7	16.7	16.7	-	-
Cellex	N + S	*7*	42.9	42.9	NA	14.3	*4*	25.0	50.0	25.0	-	-	*3*	66.7	33.3	-	-	-
Multi-G	N + RBD + S	*12*	16.7	83.3	NA	-	*2*	-	-	50.0	50.0	-	*10*	60.0	40.0	-	-	-
SureScreen	N + RBD	*12*	8.3	91.7	NA	-	*1*	-	100.0	-	-	-	*11*	72.7	9.1	18.2	-	-
StrongStep	N + S	*13*	7.7	92.3	NA	-	*1*	-	-	100.0	-	-	*12*	58.3	16.7	25.0	-	-
QuickZen	RBD	*24*	8.3	87.5	NA	4.2	*3*	100.0	-	-	-	-	*21*	47.6	33.3	19.0	-	-
Biohit	N	*34*	-	91.2	NA	8.8	*3*	33.3	-	66.7	-	-	*31*	48.4	19.4	32.3	-	-
Singuway	N + RBD	*44*	-	93.2	NA	6.8	*3*	33.3	66.7	-	-	-	*41*	41.5	31.7	26.8	-	-
Panbio	N	*39*	30.8	59.0	NA	10.3	*16*	25.0	25.0	31.3	18.8	-	*23*	39.1	39.1	21.7	-	-
Dynamiker	N + S	*73*	4.1	84.9	NA	11.0	*11*	63.6	9.1	27.3	-	-	*62*	56.5	16.1	24.2	3.2	-
Healgen	S	*76*	15.8	68.4	NA	15.8	*24*	37.5	20.8	25.0	8.3	8.3	*52*	46.2	25.0	19.2	7.7	1.9
Wantai	S	*85**	NA	NA	100.0	NA	*NA*	NA	NA	NA	NA	NA	*NA*	NA	NA	NA	NA	NA
Boson	N	*116*	6.0	84.5	NA	9.5	*18*	50.0	11.1	33.3	5.6	-	*98*	32.7	23.5	26.5	17.3	-
All RDTs combined		*545*	8.1	67.9	15.6	8.4	*90*	40.0	20.0	30.0	7.8	2.2	*370*	45.7	24.3	23.5	6.2	0.3