

Supplementary Table 1. Characteristics of the study participants in the healthy safety population	
Intradermal	
Numbers of participants	59
Male sex	30 (50.8)
Han Chinese	59 (100.0)
Age (y)	13.7 (1.5)
Intramuscular	
Number of participants	119
Male sex	65 (54.6)
Han Chinese	119 (100.0)
Age (y)	14.3 (17.6)
Values are either counts (%) or means (standard deviations)	

Supplementary Table 2. Humoral immunogenicity outcomes against wild type SARS-CoV-2 at baseline in the evaluable and expanded analysis populations

Variables	Intramuscular	Intradermal	P
	Pre-dose 1	Pre-dose 1	
S-RBD IgG on ELISA (evaluable)			
N	119	54	
GM OD450 value (95% CI)	0.250 (0.250-0.250)	0.250 (0.250-0.250)	NA
%positive (\geq LOD at 0.3)	0.0	0.0	> 0.9999
S-RBD ACE2-blocking antibody on sVNT (evaluable)			
N	119	54	
GM% inhibition (95% CI)	15.0 (15.0-15.0)	15.0 (15.0-15.0)	NA
%positive (\geq LOQ at 30%)	0.0	0.0	> 0.9999
S-RBD IgG on ELISA (expanded)			
N	119	59	
GM OD450 value (95% CI)	0.250 (0.250-0.250)	0.250 (0.250-0.250)	NA
%positive (\geq LOD at 0.3)	0.0	0.0	> 0.9999
S-RBD ACE2-blocking antibody on sVNT (expanded)			
N	119	59	
GM% inhibition (95% CI)	15.0 (15.0-15.0)	15.0 (15.0-15.0)	NA
%positive (\geq LOQ at 30%)	0.0	0.0	> 0.9999
<p>SARS-CoV-2 severe acute respiratory syndrome coronavirus 2, S spike protein, RBD receptor-binding domain, IgG immunoglobulin G, ELISA enzyme-linked immunosorbent assay, N nucleocapsid protein, GM geometric mean, OD optical density, LOD limit of detection, LOQ limit of quantification, CI confidence interval, ACE2 angiotensin-converting enzyme 2, sVNT surrogate virus neutralization test, NA not applicable. P values compare the proportion of positive responses between intramuscular and intradermal administration by Fisher's exact test</p>			

Supplementary Table 3. Humoral immunogenicity outcomes against wild type SARS-CoV-2 post-dose 2 and post-dose 3 of CoronaVac in the expanded analysis population

Variables	Intramuscular		Intradermal	
	2 doses	3 doses	2 doses	3 doses
S IgG on ELISA				
N	116	77	47	37
GM OD450 value (95% CI)	0.536 (0.493-0.582)	0.872 (0.785-0.968)	0.634 (0.562-0.716)	1.050 (0.983-1.120)
%positive (\geq LOD at 0.3)	94.0	97.4	95.7, $P > 0.9999$	100, $P > 0.9999$
S-RBD IgG on ELISA				
N	119	82	59	43
GM OD450 value (95% CI)	1.200 (1.100-1.310)	1.69 (1.600-1.780)	2.15 (2.030-2.280)	2.43 (2.310-2.560)
%positive (\geq LOD at 0.5)	96.6	100.0	100.0, $P = 0.303$	100.0, $P > 0.9999$
S-RBD ACE2-blocking antibody on sVNT				
N	119	82	59	43
GM% inhibition (95% CI)	71.2 (66.7-76.0)	84.0 (81.0-87.1)	78.2 (74.5-82.1)	90.7 (87.5-94.0)
%positive (\geq LOQ at 30%)	96.6	100.0	100.0, $P = 0.303$	100.0, $P > 0.9999$
Neutralizing antibody on PRNT				
N	119	82	59	43
GM PRNT90 (95% CI)	9.8 (8.7-11.1)	18.2 (14.5-22.9)	10.9 (8.39-14.1)	37.5 (26.8-52.4)
%positive (\geq LOD at 10)	65.6	80.5	62.7, $P = 0.741$	97.7, $P = 0.0061$
GM PRNT50 (95% CI)	26.8 (23.0-31.1)	54.2 (44.3-66.5)	30.5 (24.1-38.6)	105.0 (78.9-140.0)
%positive (\geq LOD at 10)	96.6	100.0	98.3, $P > 0.9999$	100, $P > 0.9999$
S IgG avidity on ELISA				
N	109	75	45	37
GM avidity index (95% CI)	20.5 (19.1-22.1)	35.6 (32.5-39.1)	7.0 (5.0-9.6)	52.6 (47.7-58.1)
S IgG FcγRIIIa-binding on ELISA				
N	116	77	47	37
GM OD450 value (95% CI)	0.749 (0.649-0.864)	1.300 (1.140-1.490)	1.100 (0.955-1.270)	1.780 (1.700-1.870)
%positive (\geq LOD at 0.28)	87.1	97.4	95.7, $P = 0.156$	100.0, $P > 0.9999$
SARS-CoV-2 severe acute respiratory syndrome coronavirus 2, S spike protein, N nucleocapsid protein, IgG immunoglobulin G, ELISA enzyme-linked immunosorbent assay, IgG immunoglobulin G, GM geometric mean, OD optical density, LOD limit of detection, LOQ limit of quantification, CI confidence interval, ACE2 angiotensin-converting enzyme 2, sVNT surrogate virus neutralization test, PRNT plaque reduction neutralization titer, Fc γ RIIIa Fc gamma receptor III-a. P values compare the proportion of positive responses between intramuscular and intradermal administration by Fisher's exact test				

Supplementary Table 4. Cellular immunogenicity outcomes against wild type SARS-CoV-2 S, N and M peptide pools at baseline in the evaluable and expanded analysis populations

Variables	Intramuscular	Intradermal	P
	Pre-dose 1	Pre-dose 1	
Total SNM-specific T-cell responses on flow cytometry			
N	59	47	
GM% IFN- γ ⁺ CD4 ⁺ T cells (95% CI)	0.016 (0.012-0.021)	0.022 (0.014-0.032)	0.177
%positive (\geq cut-off at 0.0075%)	83.3	81.3	0.804
GM% IL-2 ⁺ CD4 ⁺ T cells (95% CI)	0.015 (0.012-0.018)	0.019 (0.013-0.027)	0.211
%positive (\geq cut-off at 0.0075%)	83.3	79.2	0.624
GM% IFN- γ ⁺ CD8 ⁺ T cells (95% CI)	0.016 (0.012-0.022)	0.022 (0.015-0.033)	0.225
%positive (\geq cut-off at 0.0075%)	65.0	62.5	0.842
GM% IL-2 ⁺ CD8 ⁺ T cells (95% CI)	0.014 (0.012-0.017)	0.023 (0.015-0.034)	0.014
%positive (\geq cut-off at 0.0075%)	58.3	68.8	0.318
S-specific T-cell responses on flow cytometry			
N	60	48	
GM% IFN- γ ⁺ CD4 ⁺ T cells (95% CI)	0.006 (0.004-0.008)	0.005 (0.003-0.007)	0.559
%positive (\geq cut-off at 0.0075%)	35.0	25.0	2.298
GM% IL-2 ⁺ CD4 ⁺ T cells (95% CI)	0.005 (0.004-0.007)	0.004 (0.003-0.006)	0.131
%positive (\geq cut-off at 0.0075%)	48.3	16.7	0.001
GM% IFN- γ ⁺ CD8 ⁺ T cells (95% CI)	0.004 (0.003-0.005)	0.005 (0.003-0.007)	0.449
%positive (\geq cut-off at 0.0075%)	16.7	22.9	0.469
GM% IL-2 ⁺ CD8 ⁺ T cells (95% CI)	0.004 (0.003-0.005)	0.004 (0.003-0.006)	0.916
%positive (\geq cut-off at 0.0075%)	26.7	20.8	0.507
N-specific T-cell responses on flow cytometry			
N	59	47	
GM% IFN- γ ⁺ CD4 ⁺ T cells (95% CI)	0.003 (0.002-0.004)	0.005 (0.004-0.008)	0.006
%positive (\geq cut-off at 0.0075%)	10.2	27.7	0.024
GM% IL-2 ⁺ CD4 ⁺ T cells (95% CI)	0.003 (0.003-0.004)	0.005 (0.003-0.007)	0.053
%positive (\geq cut-off at 0.0075%)	18.6	23.4	0.632
GM% IFN- γ ⁺ CD8 ⁺ T cells (95% CI)	0.004 (0.003-0.005)	0.006 (0.004-0.010)	0.096
%positive (\geq cut-off at 0.0075%)	17.0	27.7	0.237
GM% IL-2 ⁺ CD8 ⁺ T cells (95% CI)	0.003 (0.003-0.004)	0.007 (0.003-0.005)	0.001
%positive (\geq cut-off at 0.0075%)	17.0	36.2	0.027
M-specific T-cell responses on flow cytometry			
N	59	47	
GM% IFN- γ ⁺ CD4 ⁺ T cells (95% CI)	0.004 (0.003-0.006)	0.005 (0.003-0.006)	0.679
%positive (\geq cut-off at 0.0075%)	23.3	23.4	> 0.9999
GM% IL-2 ⁺ CD4 ⁺ T cells (95% CI)	0.004 (0.003-0.005)	0.004 (0.003-0.005)	0.947
%positive (\geq cut-off at 0.0075%)	32.3	19.2	0.183
GM% IFN- γ ⁺ CD8 ⁺ T cells (95% CI)	0.004 (0.003-0.005)	0.004 (0.003-0.006)	0.703
%positive (\geq cut-off at 0.0075%)	17.9	14.9	> 0.9999
GM% IL-2 ⁺ CD8 ⁺ T cells (95% CI)	0.004 (0.003-0.005)	0.004 (0.003-0.006)	0.819
%positive (\geq cut-off at 0.0075%)	33.9	19.2	0.125
SARS-CoV-2 severe acute respiratory syndrome coronavirus 2, S spike, N nucleocapsid protein, M membrane protein, GM geometric mean, IFN- γ interferon-gamma, IL-2 interleukin-2, CI confidence interval. P values compare the proportion of positive responses between intramuscular and intradermal administration by Fisher's exact test			

Supplementary Table 5. Cellular immunogenicity outcomes against wild type SARS-CoV-2 S, N and M peptide pools post-dose 2 and post-dose 3 of CoronaVac in the expanded analysis population

Variables	Intramuscular		Intradermal	
	2 doses	3 doses	2 doses	3 doses
Total S, N, M-specific T-cell responses on flow cytometry				
N	60	69	48	41
GM% IFN- γ ⁺ CD4 ⁺ T cells (95% CI)	0.058 (0.040-0.083)	0.068 (0.044-0.104)	0.107 (0.063-0.183)	0.107 (0.056-0.204)
%positive (\geq cut-off at 0.0075%)	83.3	73.9	81.3, <i>P</i> = 0.804	78.1, <i>P</i> = 0.656
GM% IL-2 ⁺ CD4 ⁺ T cells (95% CI)	0.040 (0.030-0.052)	0.079 (0.055-0.112)	0.112 (0.068-0.183)	0.142 (0.078-0.258)
%positive (\geq cut-off at 0.0075%)	83.3	81.2	79.2, <i>P</i> = 0.624	80.5, <i>P</i> > 0.9999
GM% IFN- γ ⁺ CD8 ⁺ T cells (95% CI)	0.050 (0.033-0.077)	0.064 (0.038-0.107)	0.059 (0.033-0.104)	0.064 (0.033-0.124)
%positive (\geq cut-off at 0.0075%)	65.0	59.4	62.5, <i>P</i> = 0.842	63.4, <i>P</i> = 0.692
GM% IL-2 ⁺ CD8 ⁺ T cells (95% CI)	0.017 (0.014-0.022)	0.039 (0.026-0.057)	0.050 (0.031-0.803)	0.067 (0.035-0.127)
%positive (\geq cut-off at 0.0075%)	58.3	60.9	68.8, <i>P</i> = 0.318	65.9, <i>P</i> = 0.685
S-specific T-cell responses on flow cytometry				
N	60	70	48	42
GM% IFN- γ ⁺ CD4 ⁺ T cells (95% CI)	0.023 (0.015-0.036)	0.015 (0.010-0.024)	0.022 (0.012-0.040)	0.027 (0.014-0.051)
%positive (\geq cut-off at 0.005%)	70.0	54.3	58.3, <i>P</i> = 0.229	69.1, <i>P</i> = 0.164
GM% IL-2 ⁺ CD4 ⁺ T cells (95% CI)	0.015 (0.011-0.020)	0.018 (0.011-0.027)	0.020 (0.012-0.035)	0.032 (0.017-0.059)
%positive (\geq cut-off at 0.005%)	73.3	60.0	60.4, <i>P</i> = 0.214	69.1, <i>P</i> = 0.419
GM% IFN- γ ⁺ CD8 ⁺ T cells (95% CI)	0.014 (0.009-0.024)	0.017 (0.010-0.029)	0.014 (0.008-0.025)	0.010 (0.006-0.0197)
%positive (\geq cut-off at 0.005%)	48.3	48.6	45.8, <i>P</i> = 0.848	40.5, <i>P</i> = 0.439
GM% IL-2 ⁺ CD8 ⁺ T cells (95% CI)	0.006 (0.005-0.008)	0.010 (0.006-0.015)	0.012 (0.007-0.020)	0.010 (0.006-0.018)
%positive (\geq cut-off at 0.005%)	48.3	45.7	52.1, <i>P</i> = 0.847	41.5, <i>P</i> = 0.696
N-specific T-cell responses on flow cytometry				
N	60	69	48	41
GM% IFN- γ ⁺ CD4 ⁺ T cells (95% CI)	0.011 (0.008-0.017)	0.013 (0.008-0.022)	0.022 (0.011-0.043)	0.022 (0.011-0.044)
%positive (\geq cut-off at 0.005%)	55.0	50.7	54.2, <i>P</i> > 0.9999	58.5, <i>P</i> = 0.438
GM% IL-2 ⁺ CD4 ⁺ T cells (95% CI)	0.001 (0.009-0.018)	0.019 (0.012-0.029)	0.028 (0.015-0.053)	0.028 (0.014-0.055)
%positive (\geq cut-off at 0.005%)	66.7	60.9	60.4, <i>P</i> = 0.549	63.4, <i>P</i> = 0.841
GM% IFN- γ ⁺ CD8 ⁺ T cells (95% CI)	0.008 (0.005-0.012)	0.013 (0.008-0.023)	0.016 (0.008-0.031)	0.012 (0.006-0.025)
%positive (\geq cut-off at 0.005%)	31.7	39.1	43.8, <i>P</i> = 0.232	39.0, <i>P</i> > 0.9999
GM% IL-2 ⁺ CD8 ⁺ T cells (95% CI)	0.004 (0.003-0.005)	0.009 (0.006-0.014)	0.014 (0.008-0.024)	0.014 (0.007-0.026)
%positive (\geq cut-off at 0.005%)	28.3	37.7	47.9, <i>P</i> = 0.046	48.8, <i>P</i> = 0.318
M-specific T-cell responses on flow cytometry				
N	60	70	48	41
GM% IFN- γ ⁺ CD4 ⁺ T cells (95% CI)	0.007 (0.005-0.010)	0.006 (0.004-0.010)	0.008 (0.005-0.014)	0.011 (0.005-0.022)
%positive (\geq cut-off at 0.005%)	36.7	25.7	35.4, <i>P</i> > 0.9999	34.2, <i>P</i> = 0.389
GM% IL-2 ⁺ CD4 ⁺ T cells (95% CI)	0.006 (0.004-0.007)	0.006 (0.004-0.009)	0.011 (0.006-0.019)	0.014 (0.007-0.029)
%positive (\geq cut-off at 0.005%)	46.7	27.1	41.7, <i>P</i> = 0.698	46.3, <i>P</i> = 0.061
GM% IFN- γ ⁺ CD8 ⁺ T cells (95% CI)	0.006 (0.004-0.009)	0.004 (0.003-0.007)	0.007 (0.004-0.011)	0.012 (0.006-0.023)
%positive (\geq cut-off at 0.005%)	25.0	11.4	29.2, <i>P</i> = 0.667	41.5, <i>P</i> = 0.0004
GM% IL-2 ⁺ CD8 ⁺ T cells (95% CI)	0.004 (0.003-0.005)	0.004 (0.003-0.006)	0.005 (0.004-0.008)	0.012 (0.006-0.023)
%positive (\geq cut-off at 0.005%)	23.3	15.7	27.1, <i>P</i> = 0.662	46.3, <i>P</i> = 0.0008
SARS-CoV-2 severe acute respiratory syndrome coronavirus 2, S spike, N nucleocapsid protein, M membrane protein, GM geometric mean, IFN- γ interferon-gamma, IL-2 interleukin-2, CI confidence interval. <i>P</i> values compare the proportion of positive responses between intramuscular and intradermal administration by Fisher's exact test				

Supplementary Table 6. Unsolicited adverse events within 28 days of vaccination in the healthy safety population

Variables	Intramuscular (N = 123)	Intradermal (N = 59)	Overall (N = 182)
Summary of adverse events and severe adverse events			
Any adverse event	8 (0.065)	5 (0.085)	13 (0.071)
Grade 1	8 (0.065)	4 (0.068)	12 (0.066)
Grade 2	0 (0.000)	0 (0.000)	0 (0.000)
Grade 3	0 (0.000)	1 (0.017)	1 (0.005)
Severe	0 (0.000)	0 (0.000)	0 (0.000)
Data are number of events (events per participant). N total number of participants in the healthy safety population			