

TABLES

Table 1. Nominal and mean calculated concentrations, accuracy, and precision of the 18 analytes **in plasma**. 9-OH-RISP, 9-hydroxy-risperidone; AMI, amisulpride; ARI, aripiprazole; CLM, clomipramine; CLZ, clozapine; DULO, duloxetine; ESC, escitalopram; FLUO, fluoxetine; HALO, haloperidol; ; MIRTA, mirtazapine; MPH, methylphenidate; NCLM, norclomipramine; NCLZ, norclozapine; ODV, O-desmethyl-venlafaxine; OLAN, olanzapine; QUE, quetiapine; RISP, risperidone; VNLF, venlafaxine.

Analyte	Nominal concentration (ng/mL)	Inter-day (n=6)			Intra-day (n=6)		
		Measured concentration (mean +/- SD) (ng/mL)	Accuracy (%)	Precision (%)	Measured concentration (mean +/- SD) (ng/mL)	Accuracy (%)	Precision (%)
AMI	50	52.88 ± 4.81	105.76	9.09	50.30 ± 2.53	100.60	7.02
	150	142.43 ± 17.94	94.95	12.62	138.97 ± 6.14	92.65	4.42
	300	268.27 ± 19.20	89.42	7.16	273.82 ± 23.14	91.27	8.45
	900	804.54 ± 25.46	89.39	3.16	778.02 ± 91.96	86.45	11.82
ARI	50	53.41 ± 3.05	106.82	5.71	50.33 ± 3.60	100.66	7.15
	150	140.34 ± 11.37	93.56	8.10	139.91 ± 3.26	93.27	2.33
	300	293.39 ± 35.60	97.80	12.13	273.03 ± 24.16	91.01	8.85
	900	811.47 ± 81.59	90.16	10.05	818.63 ± 85.66	90.96	10.46
CLM	50	52.83 ± 2.55	105.66	4.82	51.56 ± 2.83	103.30	5.47
	150	139.74 ± 12.56	93.16	8.99	157.23 ± 9.34	104.82	5.94
	300	303.10 ± 19.71	101.03	6.50	301.78 ± 24.05	100.59	7.97
	900	861.11 ± 119.26	95.68	13.85	819.10 ± 43.89	91.01	5.36

NCLM	50	53.99 ± 3.76	107.98	6.96	53.41 ± 1.68	106.82	3.14
	150	160.62 ± 15.68	107.08	9.76	170.33 ± 8.24	113.55	4.84
	300	323.51 ± 32.36	107.84	10.00	320.42 ± 20.76	106.81	6.48
	900	915.78 ± 102.50	101.75	11.19	845.78 ± 99.35	93.98	11.75
CLZ	50	53.16 ± 2.00	106.32	3.76	46.96 ± 2.55	93.92	5.43
	150	139.89 ± 5.88	93.26	4.20	150.37 ± 9.29	100.25	6.18
	300	299.48 ± 20.81	99.83	6.95	313.80 ± 21.52	104.60	6.86
	900	873 ± 56.16	97.00	6.43	827.07 ± 58.84	91.90	7.11
NCLZ	50	51.82 ± 5.21	103.64	10.05	44.15 ± 2.35	88.30	5.33
	150	151.47 ± 15.81	100.98	10.44	146.53 ± 18.31	97.69	12.50
	300	299.87 ± 17.04	99.96	5.68	287.82 ± 37.63	95.94	13.07
	900	890.70 ± 75.31	98.97	8.46	812.63 ± 41.14	90.29	5.06
DULO	7.5	8.05 ± 0.38	107.33	4.69	7.68 ± 0.58	102.40	7.59
	22.5	22.37 ± 1.26	99.42	5.64	22.45 ± 2.83	99.78	12.58
	45	43.70 ± 4.75	97.11	10.88	47.70 ± 2.43	106.00	5.09
	135	134.75 ± 6.55	99.81	4.86	138.25 ± 6.49	102.41	4.69
ESC	7.5	8.10 ± 0.45	108.00	5.51	7.65 ± 0.55	102.00	7.15
	22.5	21.12 ± 1.48	93.87	7.01	20.88 ± 1.67	92.80	8.02
	45	42.52 ± 5.50	94.49	12.94	40.77 ± 2.07	90.60	5.09
	135	123.32 ± 6.43	91.35	5.21	132.75 ± 11.78	98.33	8.88
FLUO	50	53.36 ± 4.17	106.72	7.81	49.28 ± 1.91	98.56	3.87
	150	150.36 ± 15.41	100.24	10.25	140.72 ± 11.48	93.81	8.16
	300	302.41 ± 32.11	100.80	10.62	278.68 ± 22.14	92.89	7.94
	900	863.05 ± 30.02	95.89	3.59	824.73 ± 46.43	91.64	5.63
HALO	0.75	0.74 ± 0.06	98.67	7.60	0.74 ± 0.06	98.67	7.61
	2.25	2.42 ± 0.26	107.56	10.92	2.22 ± 0.24	98.67	10.84
	4.5	4.19 ± 0.30	93.11	7.07	4.37 ± 0.28	97.11	6.42
	13.5	12.59 ± 1.40	93.26	11.11	12.02 ± 1.32	89.04	10.96

MPH	2.5	2.50 ± 0.24	100.00	9.65	2.78 ± 0.34	111.20	4.59
	7.5	7.54 ± 0.73	100.53	9.62	7.11 ± 0.32	94.80	4.54
	15	16.13 ± 1.56	107.53	9.68	16.27 ± 1.08	108.47	6.62
	45	43.09 ± 5.45	95.76	12.66	42.06 ± 3.21	93.47	7.64
MIRTA	7.5	8.21 ± 0.44	109.47	5.41	8.48 ± 0.32	113.07	3.75
	22.5	21.42 ± 1.50	95.20	7.01	21.85 ± 1.78	97.11	8.15
	45	41.28 ± 3.74	91.73	9.06	39.35 ± 2.16	87.44	5.49
	135	126.75 ± 10.23	93.89	8.07	121.08 ± 4.36	89.69	3.61
OLAN	7.5	7.64 ± 0.57	101.87	7.50	7.38 ± 0.94	98.40	12.77
	22.5	22.12 ± 2.06	98.31	9.30	21.25 ± 1.59	94.44	7.49
	45	43.04 ± 3.28	95.64	7.62	44.03 ± 4.28	97.84	9.72
	135	133.63 ± 8.67	98.99	6.49	147.43 ± 10.22	109.21	6.93
QUE	50	50.68 ± 3.79	101.36	7.48	50.93 ± 2.70	101.86	5.29
	150	145.64 ± 10.89	97.09	7.48	147.67 ± 13.60	98.45	9.21
	300	294.86 ± 25.79	98.29	8.75	325.10 ± 29.52	108.37	9.08
	900	890.27 ± 63.93	98.92	7.18	872.43 ± 26.09	96.94	2.99
RISP	7.5	8.01 ± 0.66	106.80	8.28	7.28 ± 0.29	97.07	3.93
	22.5	22.46 ± 1.00	99.82	4.47	27.98 ± 1.23	97.69	5.59
	45	43.01 ± 3.84	95.58	8.93	40.98 ± 2.24	91.07	5.46
	135	133.97 ± 7.88	99.24	5.88	135.77 ± 13.11	100.57	9.66
9-OH-RISP	7.5	7.56 ± 0.48	100.80	6.33	7.46 ± 0.92	99.47	12.31
	22.5	24.71 ± 0.96	109.82	3.87	24.99 ± 0.88	111.07	3.51
	45	51.03 ± 3.98	113.40	7.79	49.19 ± 3.16	109.31	6.42
	135	138.52 ± 11.31	102.61	8.16	130.98 ± 6.08	97.02	4.64
VNLF	50	52.18 ± 4.22	104.36	8.09	47.08 ± 2.27	94.16	4.82
	150	159.98 ± 18.33	106.65	11.46	147.23 ± 11.05	98.15	7.06
	300	317.61 ± 18.13	105.87	5.71	308.43 ± 43.61	102.81	14.14
	900	899.46 ± 74.63	99.94	8.30	818.88 ± 36.78	90.99	4.44

ODV	50	49.19 ± 2.65	98.38	5.39	50.41 ± 2.54	100.82	5.04
	150	161.19 ± 8.53	107.46	5.29	163.31 ± 2.33	108.87	1.43
	300	326.17 ± 31.44	108.72	9.64	323.22 ± 15.95	107.74	4.93
	900	833.10 ± 40.68	92.57	4.88	810.05 ± 29.20	90.01	3.61

Accuracy = (mean calculated concentration/nominal concentration) x 100

Table 2. Nominal and mean calculated concentrations, accuracy, and precision of the four analytes **in milk**. ARI, aripiprazole; ESC, escitalopram; OLAN, olanzapine; QUE, quetiapine.

Analyte	Nominal concentration (ng/mL)	Inter-day (n=6)			Intra-day (n=6)		
		Measured concentration (mean +/- SD) (ng/mL)	Accuracy (%)	Precision (%)	Measured concentration (mean +/- SD) (ng/mL)	Accuracy (%)	Precision (%)
ARI	20	20.20 ± 1.47	101.02	13.76	18.62 ± 1.00	106.89	5.42
	60	65.62 ± 5.23	109.37	7.97	68.52 ± 2.08	114.20	3.03
	100	107.46 ± 4.39	107.46	4.09	110.25 ± 4.18	110.25	3.79
	300	311.50 ± 24.46	103.83	7.85	321.35 ± 14.99	107.12	4.67
ESC	2.5	2.5 ± 0.12	99.98	21.31	2.53 ± 0.23	98.65	9.19
	7.5	6.52 ± 0.41	86.94	6.34	6.68 ± 0.58	89.15	8.70
	12.5	10.96 ± 0.85	87.65	7.74	10.68 ± 0.23	85.44	2.11
	37.5	32.71 ± 2.93	87.22	8.96	34.50 ± 3.35	91.99	9.71
OLAN	2.5	2.53 ± 0.18	101.92	14.02	2.79 ± 0.17	88.47	6.23
	7.5	6.94 ± 0.52	92.59	7.42	7.10 ± 0.63	94.68	8.82
	12.5	11.34 ± 0.95	90.72	8.36	11.35 ± 1.18	90.83	10.36
	37.5	33.71 ± 3.11	89.89	9.23	32.78 ± 1.00	87.41	3.06
QUE	20	19.82 ± 1.68	99.11	11.79	20.74 ± 1.49	96.31	7.16
	60	63.54 ± 3.50	105.89	5.51	59.78 ± 2.81	99.64	4.70
	100	102.94 ± 6.08	102.94	5.90	99.59 ± 4.29	99.59	4.31
	300	313.27 ± 30.06	104.42	9.60	294.75 ± 8.79	98.25	2.98

Table 3. Stability results for 18 analytes **in plasma**. 9-OH-RISP, 9-hydroxy-risperidone; AMI, amisulpride; ARI, aripiprazole; CLM, clomipramine; CLZ, clozapine; DULO, duloxetine; ESC, escitalopram; FLUO, fluoxetine; HALO, haloperidol; MIRTA, mirtazapine; MPH, methylphenidate; NCLM, norclomipramine; NCLZ, norclozapine; ODV, O-desmethyl-venlafaxine; OLAN, olanzapine; QUE, quetiapine; RISP, risperidone; VNFL, venlafaxine.

Analyte	Nominal concentration (ng/mL)	At room temperature for 4 h (n=2)		After two freeze thaw cycles at -35 °C (n=2)		After two months at -80 °C (n=2)	
		Measured concentration (ng/mL)	Concentration difference (%)	Measured concentration (ng/mL)	Concentration difference (%)	Measured concentration (ng/mL)	Concentration difference (%)
AMI	150	151.56	1.04	130.32	-13.12	153.40	2.27
	300	283.57	-5.48	305.66	1.89	292.50	-2.50
	900	907.23	0.80	821.7	-8.70	867.25	-3.64
ARI	150	167.64	11.76	170.82	13.88	169.40	12.93
	300	313.88	4.63	297.56	-0.81	338.10	12.70
	900	861.89	-4.23	925.5	2.83	1016.40	12.93
CLM	150	140.24	-6.51	150.90	0.60	171.85	14.57
	300	268.35	-10.55	283.24	-5.59	330.90	10.30
	900	838.01	-6.89	814.7	-9.48	980.10	8.90
NCLM	150	154.25	2.83	157.49	4.99	159.58	6.38
	300	284.38	-5.21	275.24	-8.26	297.55	-0.82
	900	795.10	-11.66	785.9	-12.68	1015.29	12.81
CLZ	150	146.17	-2.55	159.71	6.47	163.35	0.30
	300	297.46	-0.85	311.37	3.79	338.55	11.44
	900	841.86	-6.46	885.5	-1.61	1006.68	11.85
NCLZ	150	129.74	-13.51	143.24	-4.51	160.95	7.30
	300	292.35	-2.55	292.50	-2.50	333.35	11.12

	900	807.11	-10.32	778.8	-13.47	928.45	3.16
DULO	22.5	24.64	9.49	24.87	10.53	23.70	5.33
	45	46.70	3.77	51.33	14.07	47.80	6.22
	135	142.30	5.41	151.0	11.86	145.90	8.07
ESC	22.5	22.82	1.42	21.50	-4.44	22.60	-3.62
	45	38.59	-14.26	45.46	1.01	39.60	-7.80
	135	123.26	-8.70	122.8	-9.02	141.30	4.67
FLUO	150	142.74	-4.84	152.67	1.78	170.85	13.90
	300	263.25	-12.25	298.38	-0.54	313.15	4.38
	900	818.09	-9.10	796.8	-11.46	1029.25	14.36
HALO	2.25	2.57	14.23	2.36	4.67	2.45	8.89
	4.5	4.83	7.33	5.05	12.11	4.65	3.33
	13.5	14.87	10.78	15.0	11.00	13.05	-3.33
MIRTA	22.5	22.63	0.58	24.08	7.02	20.25	-10.00
	45	43.56	-3.21	45.84	1.87	42.75	-5.00
	135	130.57	-3.28	142.1	5.23	138.10	2.30
MPH	7.5	7.73	3.07	7.66	2.09	6.58	-12.33
	15	15.07	0.44	14.78	-1.44	13.10	-12.67
	45	41.46	-7.86	43.91	-2.43	40.65	-9.67
OLAN	22.5	23.68	5.24	23.05	2.44	21.40	-4.89
	45	42.29	-6.03	43.31	-3.77	44.05	-2.11
	135	125.96	-6.70	139.9	3.64	149.40	10.67
QUE	150	151.08	0.72	153.11	2.07	166.05	10.70
	300	282.12	-5.96	309.19	3.06	290.50	-3.17
	900	774.91	-13.90	773.5	-14.06	821.61	-8.71
RISP	22.5	25.12	11.64	25.20	11.98	24.00	-0.21
	45	50.55	12.33	49.92	10.92	47.80	1.27
	135	149.79	10.96	145.7	7.94	152.15	10.65
9-OH-RISP	22.5	25.78	14.59	25.40	12.89	22.65	0.67
	45	47.93	6.50	44.58	-0.93	41.60	-7.56
	135	130.03	-3.68	126.83	-6.05	131.0	-2.96

VNLF	150	166.63	11.08	148.86	-0.76	144.95	-3.37
	300	295.06	-1.65	343.45	14.48	337.50	12.50
	900	850.23	-5.53	861.7	-4.26	1011.41	12.38
ODV	150	165.53	10.35	146.28	-2.48	170	13.33
	300	341.10	13.70	306.63	2.21	330	10
	900	952.56	5.84	807.3	-10.30	976.50	8.5

Table 4. Practical application of LC-MS/MS method for TDM in plasma: Results from 2020. 9-OH-RISP, 9-hydroxy-risperidone; AMI, amisulpride; ARI, aripiprazole; CLM, clomipramine; CLZ, clozapine; DULO, duloxetine; ESC, escitalopram; FLUO, fluoxetine; HALO, haloperidol; MIRTA, mirtazapine; MPH, methylphenidate; NCLM, norclomipramine; NCLZ, norclozapine; ODV, O-desmethyl-venlafaxine; OLAN, olanzapine; QUE, quetiapine; RISP, risperidone; VNLF, venlafaxine; TRR, therapeutic reference range.

Analyte	Number of samples	Mean (ng/mL) ± SD	TRR (ng/mL)	Lower (%)	In (%)	Higher (%)
AMI	7	328 ± 170	100-300	14	14	71
ARI	47	374 ± 296	100-350	21	34	45
CLZ	341	460 ± 482	250-700	30	51	19
CLM + NCLM	4	477 ± 160	230-450	0	25	75
DULO	5	122 ± 68	30-120	0	40	60
ESC	18	26 ± 21	15-80	33	67	0
FLUO	13	285 ± 274	120-500	23	54	23
HALO	8	10 ± 4	1-10	0	50	50
MPH	7	20 ± 10	12-79	29	71	0
MIRTA	5	31 ± 31	30-80	4	0	20
NCLZ	341	233 ± 203	100-500	22	70	8
OLAN	61	45 ± 33	20-80	21	62	16

QUE	64	306 ± 295	100-500	31	47	22
RISP + 9-OH- RISP	19	75 ± 44	20-60	5	47	47
VNLF + ODV	12	271 ± 163	100-400	0	67	33
