Supporting Information to

Particle-based Investigation of Excipients Stability: The effect of storage conditions on moisture content and swelling

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Abstract

This supporting information provides further data collected during the moisture sorption/desorption analysis and the storage-induced particle size swelling.

Table S1: The recorded datalogger storage conditions

(The 25°C/30%RH represents the Laboratory equilibration condition)

Target storage condition	Actual storage condition
50°C/75%RH	49.8°C±0.3/ 77.7%RH±1.3
25°C/75%RH	24.9°C±0.4/ 77.7%RH±1.3
50°C/30%RH	49.8°C±0.3/ 32.4%RH±0.9
25°C/30%RH	20.4°C±0.6/ 26.4%RH±3.5

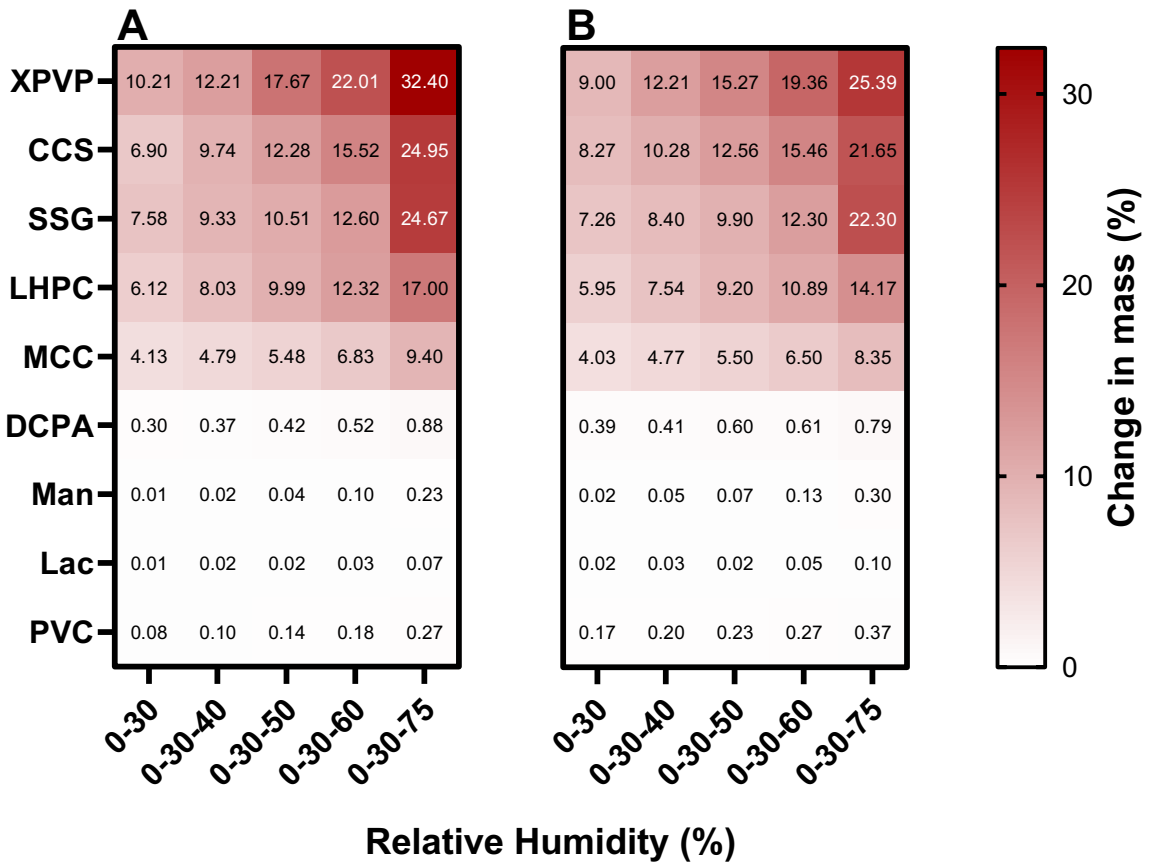


Figure S1: Moisture uptake of excipients at (A) 25°C and (B) 50°C. Changes in mass (%) were calculated relative to the dry reference mass at 0%RH. (0-30%RH represents an average of 4 measurements)

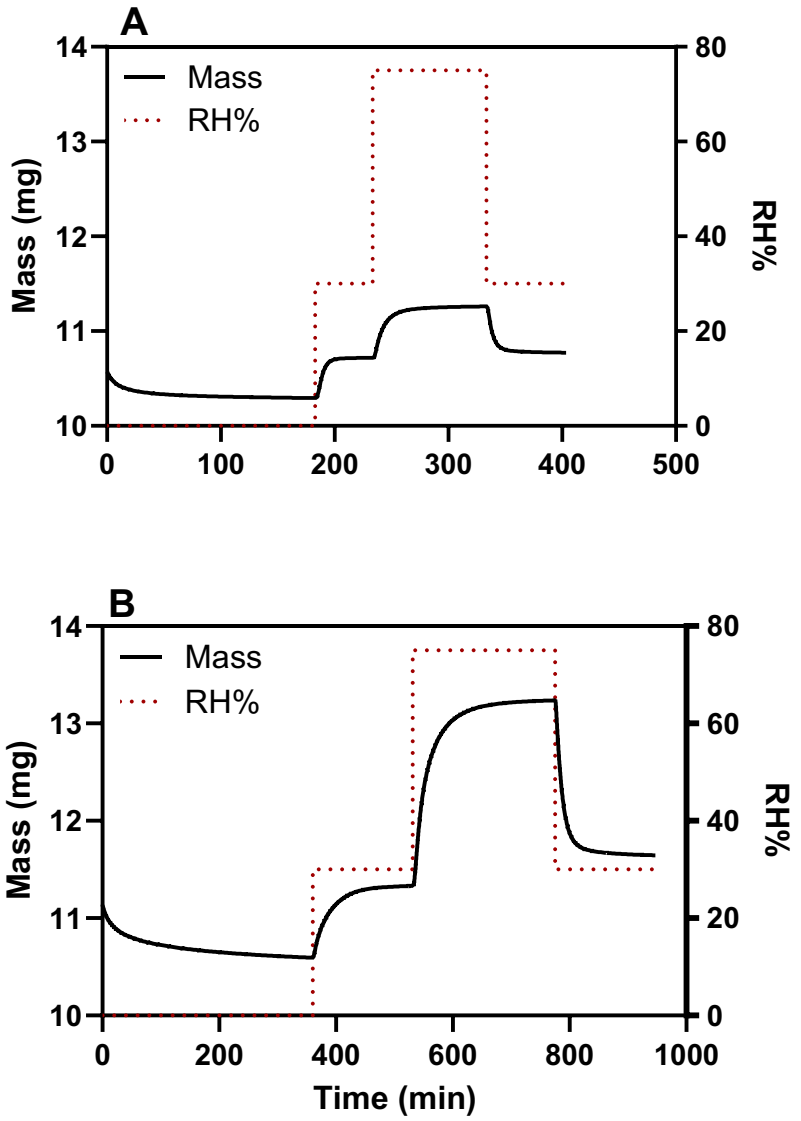


Figure S2: Moisture sorption and desorption- time profile of (A) MCC and (B)CCS at 25°C.

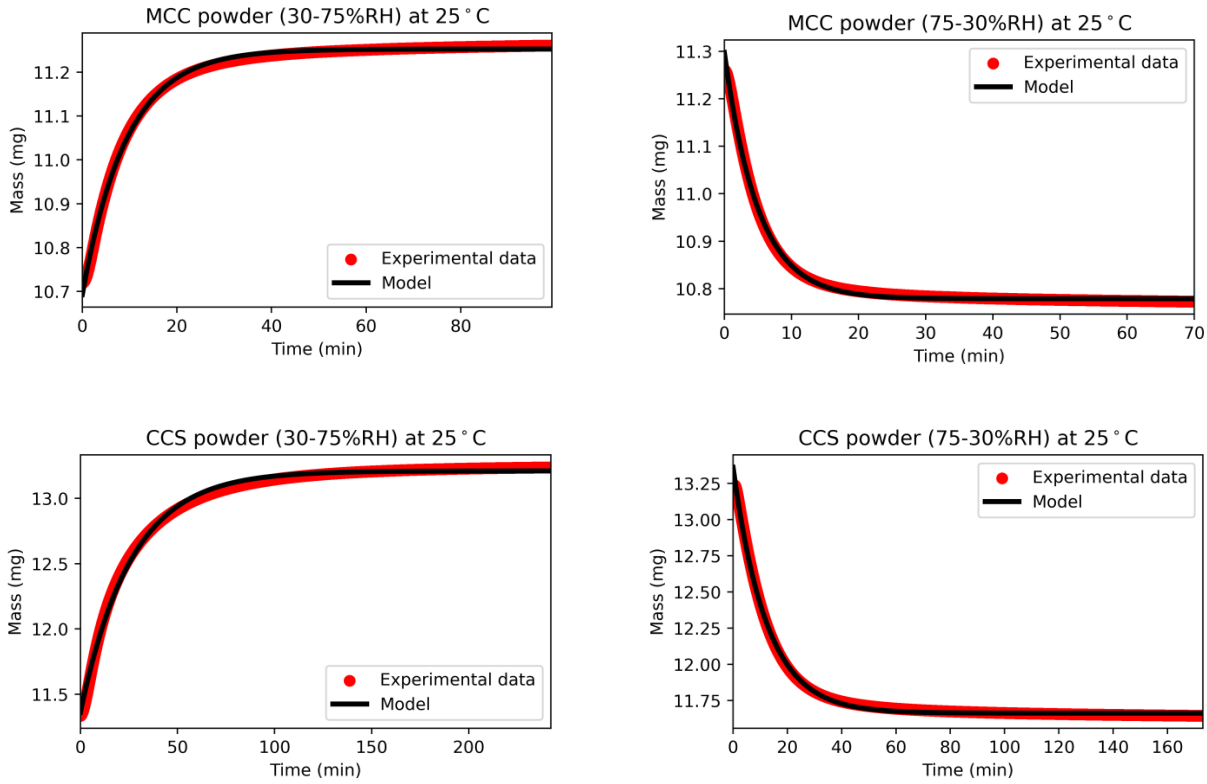


Figure S3: Moisture sorption and desorption of MCC and CCS at 25°C over time as predicted by the model vs. experimental measurements.

Table S2: The Prediction performance of moisture sorption kinetic rate constant model at 25°C (0-30%RH at the two temperatures were conducted 4 times with their corresponding rows reporting the mean and (SD))

Excipient	RH% step	r (s^{-1})	CI (±)	R^2	RMSE
Lactose	0-30	0.1799 (0.1354)	0.0054 (0.0057)	0.7159 (0.2642)	0.0004 (0.0001)
	30-40	0.3958	0.0047	0.9652	0.0001
	30-50	0.1870	0.0025	0.9725	0.0001
	30-60	0.1596	0.0018	0.9638	0.0001
	30-75	0.1812	0.0009	0.993	0.0002
L-HPC	0-30	0.0981 (0.0027)	0.0001 (8.39E-06)	0.9957 (0.0003)	0.0082 (0.0001)
	30-40	0.0510	0.0001	0.9928	0.0034
	30-50	0.0774	9.44E-05	0.9979	0.0040
	30-60	0.0819	0.0001	0.9973	0.0072
	30-75	0.0747	9.50E-05	0.99726	0.0124
SSG	0-30	0.0601 (0.0025)	0.0001 (1.33E-05)	0.9944 (0.0006)	0.0155 (0.0015)
	30-40	0.0879	9.31E-05	0.9991	0.0014
	30-50	0.1313	0.0006	0.9395	0.0143
	30-60	0.1155	0.0003	0.9927	0.0108
	30-75	0.0162	2.18E-05	0.9926	0.0330
CCS	0-30	0.0341 (0.0012)	3.4E-5 (7.8E6)	0.9975 (0.0015)	0.0071 (0.0017)
	30-40	0.0312	3.1E-5	0.9982	0.0025
	30-50	0.0564	4.4E-5	0.9989	0.0040
	30-60	0.0657	0.0001	0.9989	0.0061
	30-75	0.0384	4.7E-5	0.9951	0.0267
MCC	0-30	0.2239 (0.0092)	0.0003 (0.0001)	0.9988 (0.0006)	0.0024 (0.0010)
	30-40	0.2199	0.0005	0.9977	0.0007
	30-50	0.2343	0.0005	0.9965	0.0016
	30-60	0.1507	0.0005	0.9901	0.0046
	30-75	0.1073	0.0002	0.9971	0.0059

DCPA	0-30	0.7432 (0.0178)	0.0020 (0.0003)	0.9975 (0.0007)	0.0003 (0.0001)
	30-40	0.5365	0.0019	0.9961	0.0001
	30-50	0.4753	0.0010	0.9986	0.0001
	30-60	0.4041	0.0011	0.9975	0.0002
	30-75	0.1973	0.0003	0.9987	0.0005
Mannitol	0-30	1.0403 (0.3020)	0.0469 (0.0371)	0.7410 (0.2356)	0.0002 (1.2E-4)
	30-40	0.9518	0.0219	0.9416	4.7E-5
	30-50	0.5647	0.0032	0.9912	0.0001
	30-60	0.3072	0.0010	0.9970	0.0001
	30-75	0.2902	0.0012	0.9937	0.0004
XPVP	0-30	0.0865 (0.0289)	0.0002 (0.0001)	0.9899 (0.0053)	0.0182 (0.0031)
	30-40	0.0349	4.9E-5	0.9960	0.0054
	30-50	0.0521	3.8E-5	0.9989	0.0054
	30-60	0.0497	3.0E-5	0.9992	0.0078
	30-75	0.0414	4.0E-5	0.9973	0.0235

(*r*: kinetic rate constant, CI: confidence Interval, R^2: coefficient of determination, RMSE: Root mean square of error)

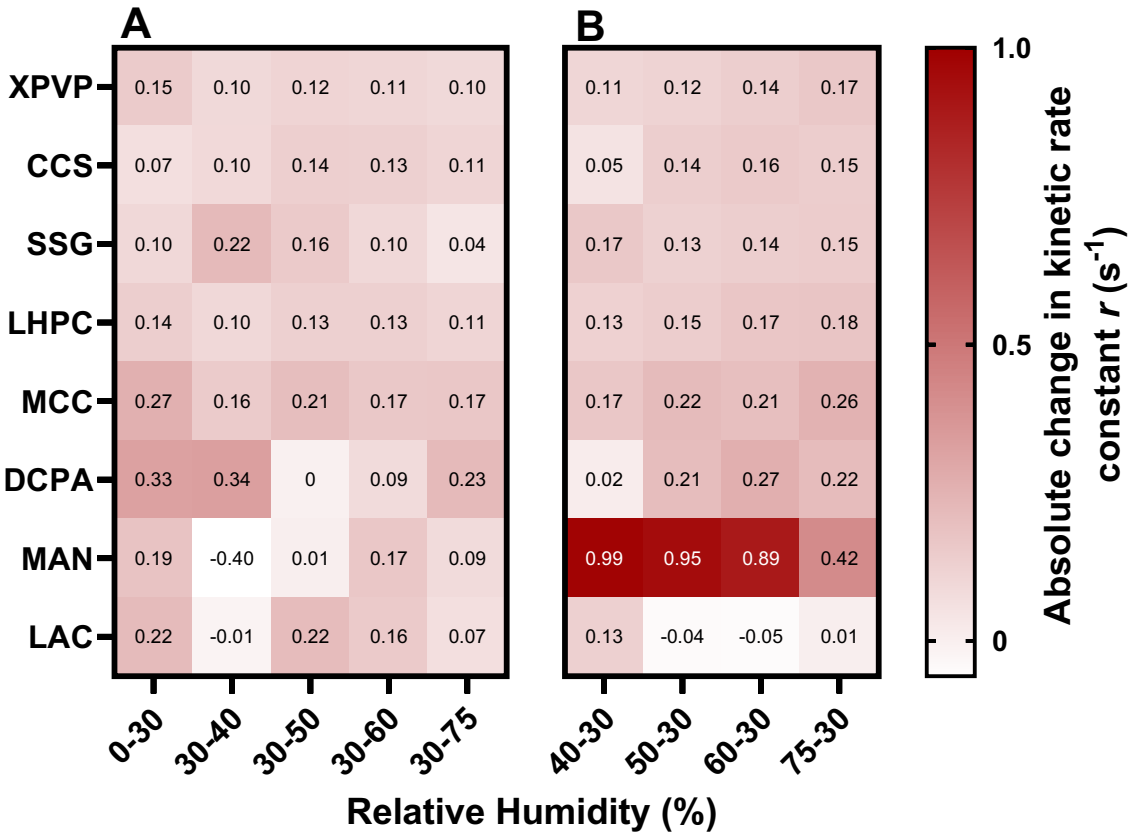
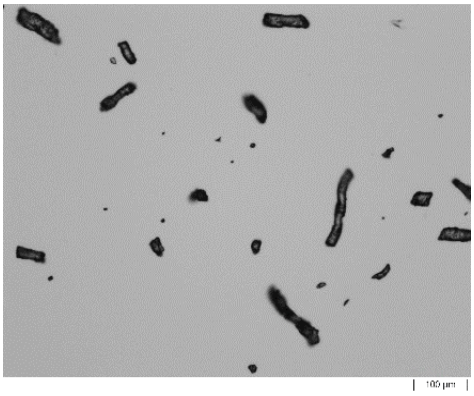
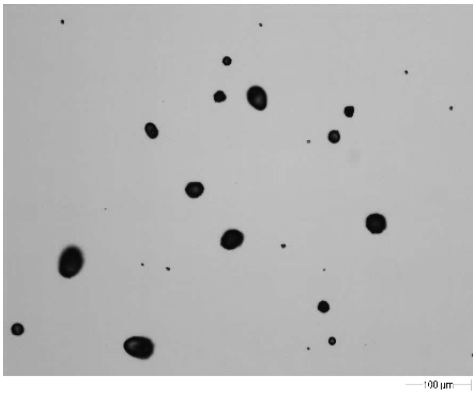


Figure S4: Absolute change in kinetic rate constant (*r*) from 25°C to 50°C of the tested excipients in (A) moisture sorption and (B) desorption as a function of RH% steps.

CCS



SSG



MCC

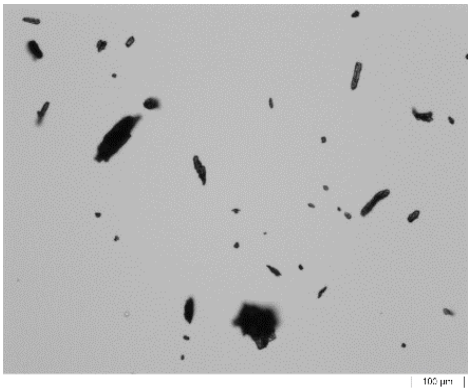


Figure S5: Field of view images of swelling excipients studied using 10X lens.

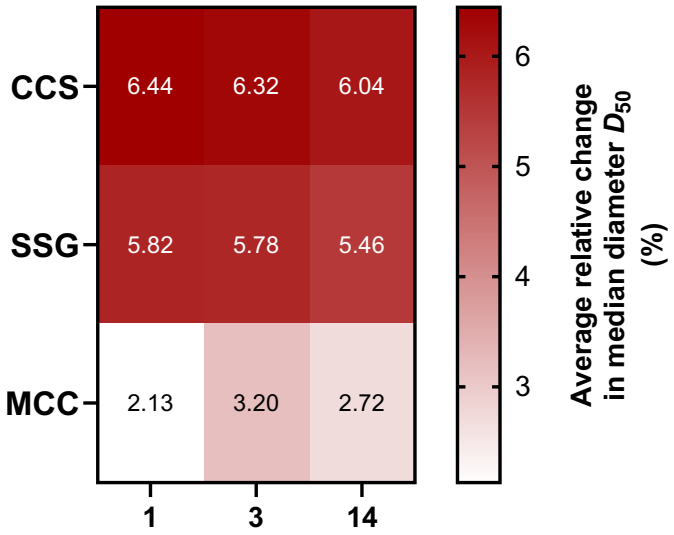


Figure S6: Relative change in volume-based diameter D_{50} of the studied excipients after storage at 50℃/30%RH, showing all time points: 1,3, and 14 days.

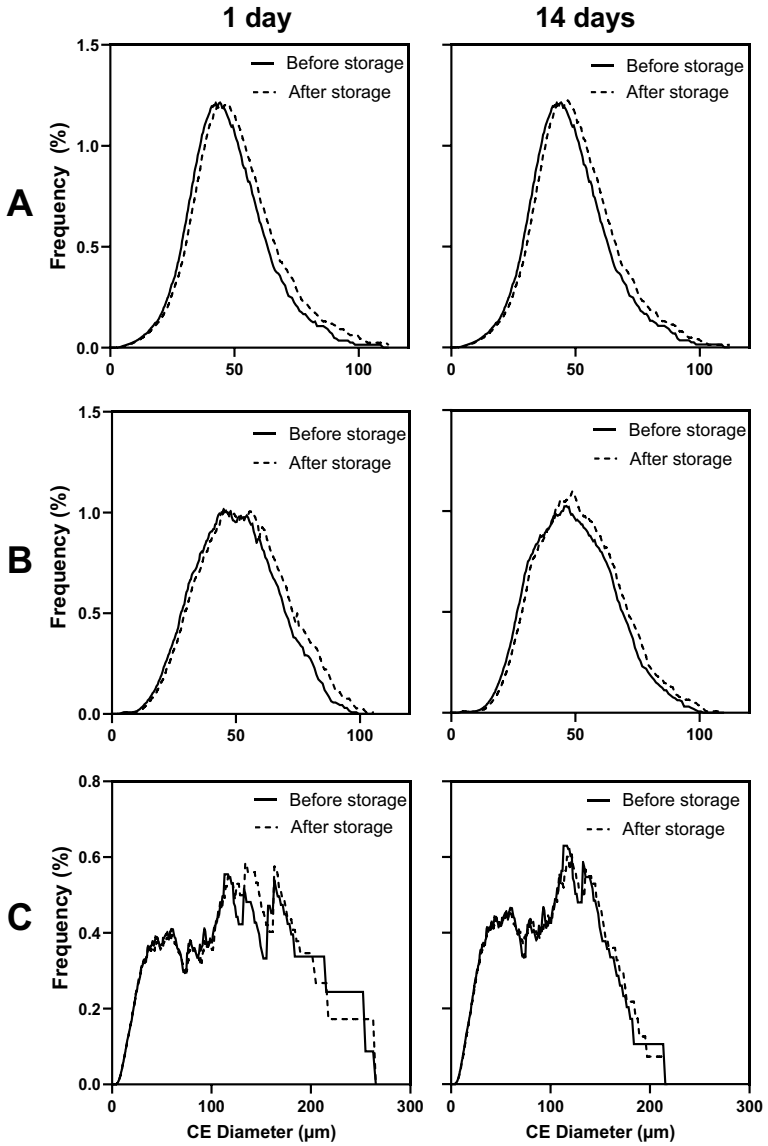


Figure S7: The change in number-based size distributions of (A) CCS, (B) SSG, and (C) MCC particles after storage at 25℃/75%RH for 1 and 14 days. (The example shown on each time point represents one of the samples analysed for this time point, CED smoothed over 50 points).

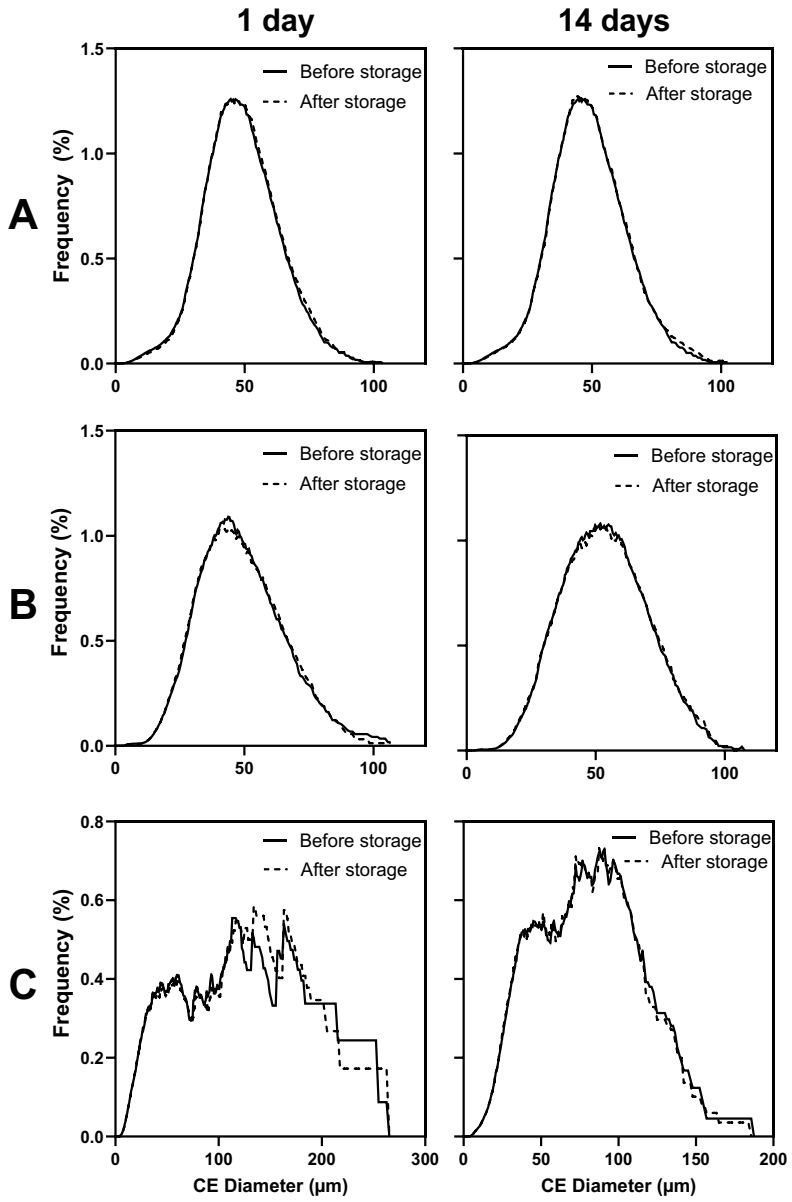


Figure S8: The change in number-based size distributions of (A) CCS, (B) SSG, and (C) MCC particles after storage at 50℃/30%RH for 1and 14 days. (The example shown on each time point represents one of the samples analysed for this time point, CED smoothed over 50 points).

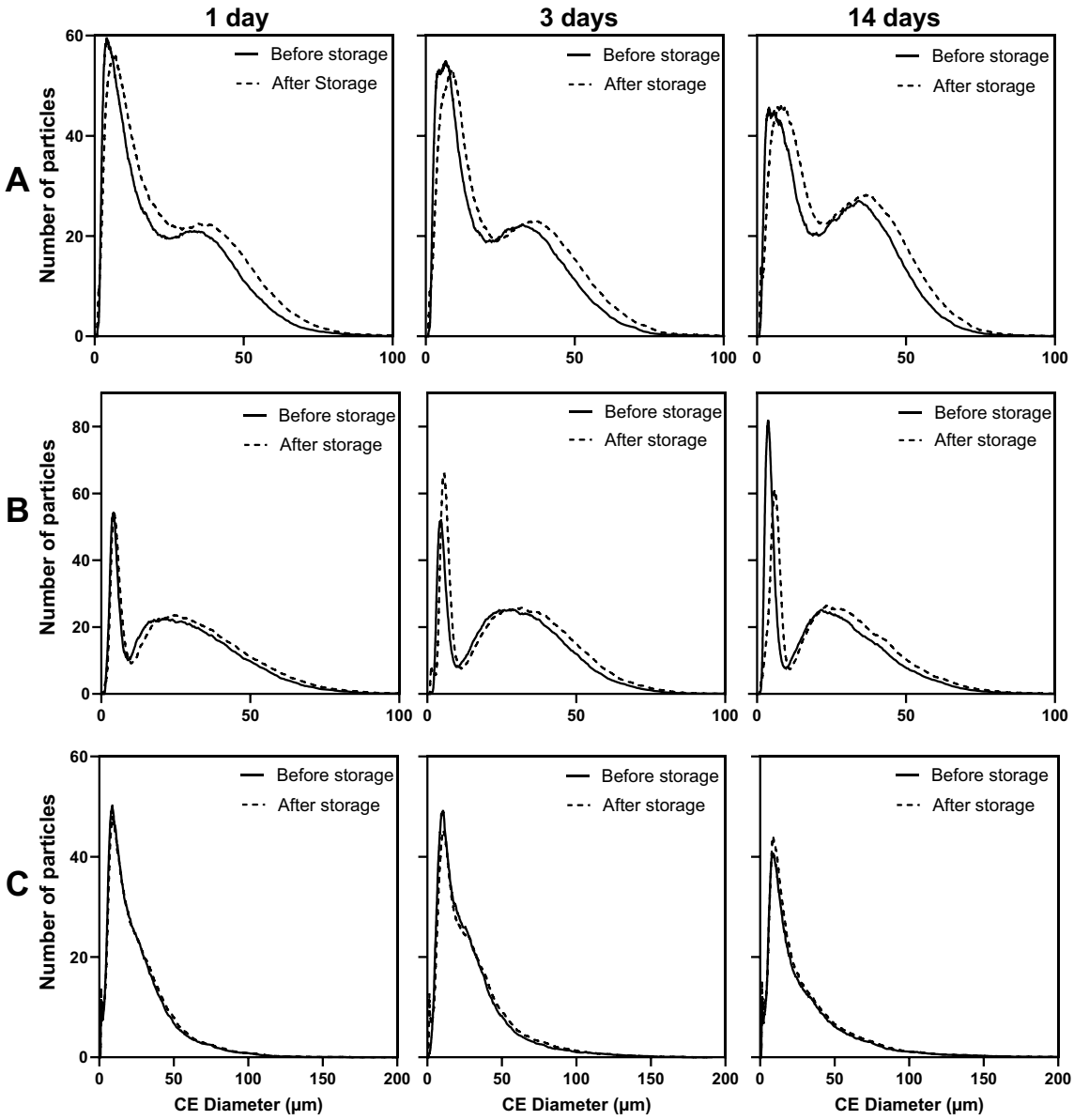
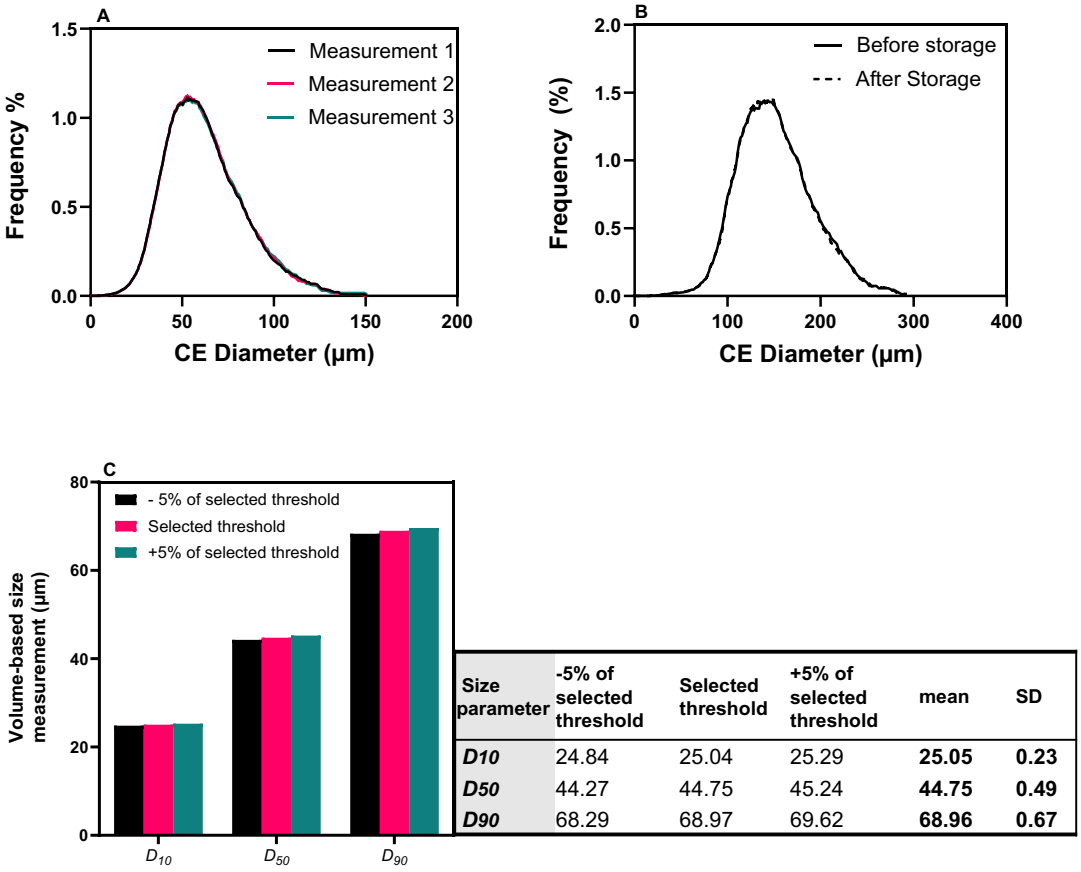


Figure S9: The change in number-based size distributions of (A) CCS, (B) SSG, and (C) MCC particles after storage at 50℃/75%RH for 1,3 and 14 days. (The example shown on each time point represents one of the samples analysed for this time point, CED smoothed over 50 points).



Size parameter	-5% of selected threshold	Selected threshold	+5% of selected threshold	mean	SD
D10	24.84	25.04	25.29	**25.05**	**0.23**
D50	44.27	44.75	45.24	**44.75**	**0.49**
D90	68.29	68.97	69.62	**68.96**	**0.67**

Figure S10: Measures to evaluate the Reliability of Morphologi4 in particle size Analysis. (A) Demonstrating the repeatability of measurements for the same sample. (B) Utilizing PVC powder as a control material after storage at 50℃/75%RH for 3 days. (C) Investigating the threshold effect on CCS particle size analysis to assess the robustness of the analysis under storage conditions.

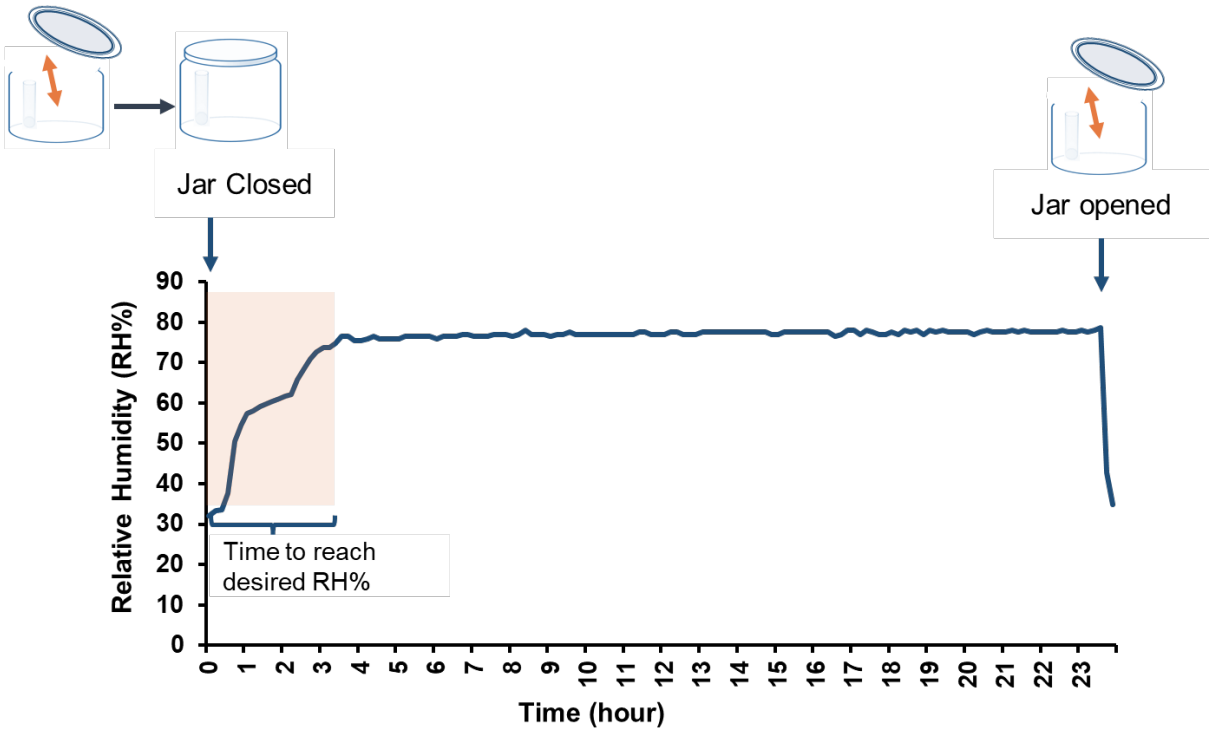


Figure S11: The time needed to establish the required 75% RH inside jars (data shown were extracted from a data logger inside one of the jars intended for 1-day storage).