Collaborative Evaluation of Commercially Available Automated Powder Dispensing Platforms for High Throughput Experimentation in Pharmaceutical Applications, Supporting Information

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1. Automated powder dispensing platform system specifications

Chemspeed SWING systems with SDU powder dispensing technology at Bristol-Myers Squibb, Merck, and Pfizer were evaluated. The Bristol-Myers Squibb and Merck systems used Chemspeed AutoSuite Editor Product Version 1.12.1.1. The Pfizer system used Chemspeed AutoSuite Editor Product Version 2.1.32.10. All three systems were located in a purge box provided by Chemspeed. The following settings were selected for all systems: Teach mode, Transfer mode set to 1-1, Optimize For set to Accuracy and Speed, Minimum FD Speed Evaluation set to Automatic Optimization. Container spanning was not used.

Mettler-Toledo Quantos QB5 systems at AstraZeneca, GlaxoSmithKline, and Pfizer were evaluated. The AstraZeneca system 1 had Balance Type QD206DR with Terminal SW 3.00 and was located in a glovebox.   The AstraZeneca system 2 was located in a fume cupboard. The GlaxoSmithKline system had Balance Type QD206DR with Terminal SW 3.40 and was located in a custom Flow Sciences local exhaust ventilation (LEV) enclosure. The Pfizer system had Balance Type XPE206DR with Terminal SW 1.00 and was located in a custom Plas-Labs purgebox. The following settings were selected for all systems: Tapper Intensity set to 50%, Tapper on/off set to On, Tapper duration set to 1 sec, Tapper before dosing set to On for fumed silica and Off for all other powders, Tapper during dispense set to On, Environment set to Standard, Value Release set to Reliable and Fast, AutoZero set to On, Weighing Mode set to Universal.

Unchained Labs Freeslate (formerly Freeslate CM3) systems at AstraZeneca, Bristol-Myers Squibb, Merck, and Pfizer were evaluated. The AstraZeneca and Pfizer systems were located in a glovebox. The Bristol-Myers Squibb and Merck systems were located on an open bench. An Unchained Labs Junior (formerly Freeslate Protégé) system located in an LEV enclosure provided by Unchained Labs was evaluated at GlaxoSmithKline. Automation Studio version 8.5.50827.4 was used at AstraZeneca, Bristol-Myers Squibb and Merck, version 8.3.10.64 at GlaxoSmithKline, and version 8.5.50217.1 at Pfizer. Firmware version 0x10033 was used on all systems. The following settings were selected for all systems: Dispense Tolerance Mode set to Percent, Dispense Tolerance Time Out set to 500 sec, Max Number of Retries set to 3, Dispense Mode Optimization set to Accuracy, Plate on balance or Vial on balance set to Plate on balance.

2. Depictions of powder dispensing systems

Figure S1. Chemspeed SWING SDU system

Figure S2. Mettler-Toledo Quantos QB5 system

QH012-LNMP
Ø2.5mm Dosing Pin
with pushing stirrer
Pinocchio 1mm nose

Figure S3. Unchained Labs Freeslate and Junior SV and Classic dispense heads

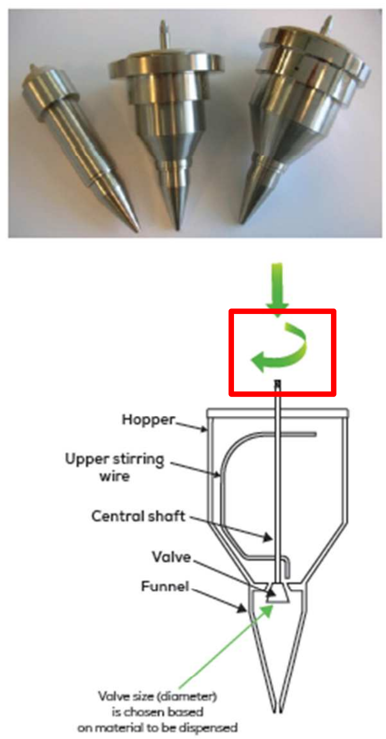

Figure 3: Powdernium™ classic powder dispensing.

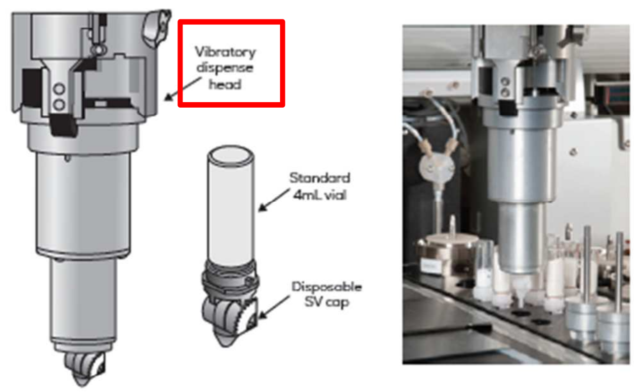

Figure 4: Powdernium SV (storage vial) dispensing.

3. Run Order Schedule

Table S1. Run order schedule for all platforms

Run #	Target dispense mass/vial (mg)	# of Dispenses/run
1	2	20
2	10	20
3*	50	20
4	10	20
5*	50	20
6	2	20
7*	50	20
8	2	20
9	10	20
		180 total dispenses (120 for fumed silica)

*Runs 3, 5 and 7 were omitted for fumed silica

4. Dispense head refill schedules

Table S2. Unchained Labs SV dispense head refill schedule

Powder	Refill point
Sodium chloride	no refill required
L-proline	refill following run 3
	refill following run 6
Fumed silica	refill following run 1
	refill following every 10 vials of run 2
	Omit run 3
	refill following every 10 vials of run 4
	Omit run 5
	refill following run 6
	Omit run 7
	refill following run 8
	refill following every 10 vials of run 9
D-Mannitol	refill following run 6
PVPP	refill following run 3
	refill following run 6
Limestone powder	refill following run 6
Thiamine HCl	refill following run 3
	refill following run 6

Table S3. Chemspeed SDU and Mettler-Toledo QH012-LNMP dispense head refill schedule

Powder	Refill point
Sodium chloride	no refill required
L-proline	no refill required
Fumed silica	refill following run 2
	Omit run 3
	Omit run 5
	refill following run 6
	Omit run 7
D-Mannitol	no refill required
PVPP	no refill required
Limestone powder	no refill required
Thiamine HCl	no refill required

5. Powder characterization tests

Testing was performed by Jacob St. Germain (Eurofins Lancaster Laboratories Inc. PSS, 2425 New Holland Pike, Lancaster, PA 17605 and Pfizer Inc., Worldwide Research and Development, Pharmaceutical Sciences Small Molecule Chemical Research and Development, Eastern Point Road, Groton, Connecticut 06340, United States) and Ka Nip Ying (Pfizer Inc., Worldwide Research and Development, Pharmaceutical Sciences Small Molecule Chemical Research and Development, Eastern Point Road, Groton, Connecticut 06340, United States).

Flow function coefficient: Powder flow behavior was measured using a Dietmer-Schulze RST-XS ring shear tester equipped with a number 1/4 shear cell.[a] Each sample was equilibrated at 50% relative humidity prior to testing. Flow function coefficient values obtained from consolidating the powder at 4 kPa are reported.[b]

Bulk and Tap density: Bulk and tap densities of powders were measured according to USP <616> method I, using a PT-TD200 standard USP tapped density apparatus from Pharma Test Apparatebau (Hainburg, Hesse, Germany).[c] Samples were tested at ambient conditions. Values are reported as g/cc.

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[a] a. For a white paper on ring shear testing see: Schulze, D. http://www.dietmar-schulze.de/grdle1.pdf b. For a multi-company and multi-university evaluation of results obtained for a single powder (limestone powder CRM-116) on two different commercial ring shear testers see: Schulze, D. *Advanced Powder Technology* **2011**, *22*, 197 – 202.

[b] The flow for sodium chloride at 4kPa was too high to be accurately measured. Its FFC was assigned the value >50.

[c] See: https://www.usp.org/sites/default/files/usp/document/harmonization/gen-chapter/bulk_density.pdf

True density: True densities of powders were determined with helium pycnometer AccuPyc II 1340 (Micromeritics, GA, USA) operated at ambient temperature. Duplicate determinations were made and mean values reported as g/cc.

Particle size analysis: Particle size analyses were conducted on a Sympatec HELOS laser diffraction instrument using dry dispersion. Triplicate determinations were made and mean D[4,3] values reported as μm. D[4,3] is also referred to as the volume mean diameter.

Dynamic Vapor Sorption: Water sorption and desorption studies were conducted on an automated vapor sorption analyzer (DVS Advantage; Surface Measurements Systems, London, UK). Approximately 10-20 mg of the powder sample were placed in a platinum sample pan and dried at ≤ 3% relative humidity (RH) and 25 °C before conducting the absorption and desorption cycles. The RH progressively increased to 90% by increments of 10%, then decreased to a final RH of 10% by decrements of 10%. "Hygroscopic onset" represents the RH at the onset of mass gain. "Hygroscopic maximum" represents the % mass gain at 90% RH.[d] "Hygroscopic final" represents the final % mass gain following the desorption cycle.

Scanning Electron Microscope: Scanning electron micrographs were obtained using a Zeiss MA-10 Scanning Electron Microscope (SEM). Samples were prepared by placing the sample onto an aluminum electron microscopy stud (Ted Pella Inc.) and sputter-coated with gold/palladium before being imaged with the SEM. Imaging conditions (i.e., accelerating voltage, working distance, and magnification) may be found on each individual image.

Dynamic Image Analysis (QicPic): Particle shape analyses were conducted on a Sympatec QicPic Dynamic Image Analyzer using dry dispersion. The Aspect Ratio is defined as the ratio between the

[d] For sodium chloride, duplicate runs were conducted and "Hygroscopic maximum" represents the mean % mass gain at 80% RH.

minimum and maximum feret diameters of a particle, where the minimum and maximum feret diameters are the shortest and longest distances respectively between two parallel tangents to the contour of the particle after considering all possible orientations. Sphericity is defined as the ratio of perimeter of a circle of equivalent area to the perimeter of the actual particle. A perfect circle has an Aspect Ratio and Sphericity equal to 1.0.[e] Triplicate determinations were made and the averages of the median Aspect Ratios (A50 values) and median Sphericity values (S50 values) are reported.

Permeability: Permeabilities of powder samples were measured on a Freeman FT4 Powder Rheometer.[f] The method utilized a vented piston to constrain a powder column under a range of applied normal stresses, while air was passed through the powder column. The relative difference in air pressure between the bottom and the top of the powder column was a function of the powder's permeability. Values from experiments using 1.00 kPa of applied stress are reported as mBar.

Compressibility: Compressibilities of powder samples were measured on a Freeman FT4 Powder Rheometer.[6] Compressibility measurements were achieved by applying increasing levels of compressive force with a piston to a conditioned powder and measuring the change in volume as a function of the applied force. Values from experiments using 0.50 kPa of applied force are reported as %.

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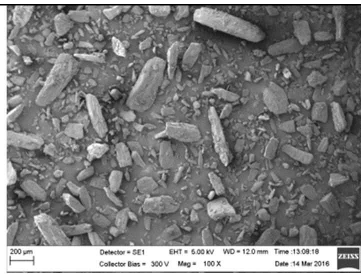
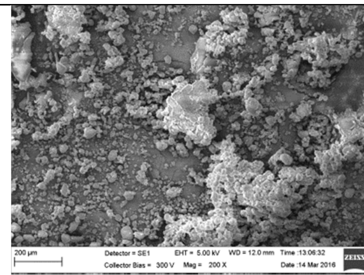
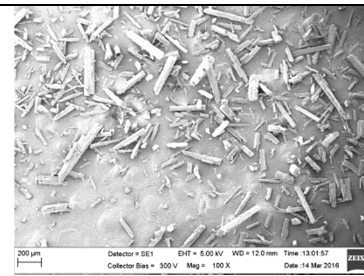
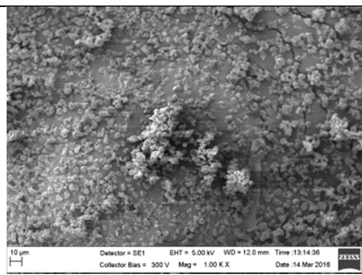
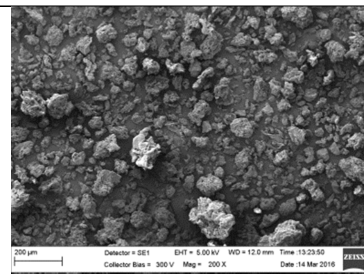
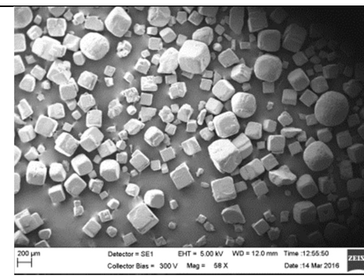
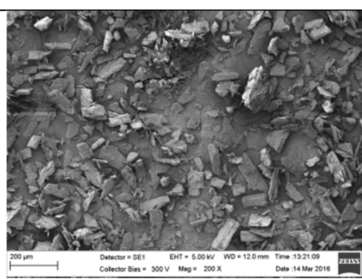
[e] Yu, W.; Lingzhi, L.; Bharadwaj, R.; Hancock, B. C., What is the "typical" particle shape of active pharmaceutical ingredients? *Powder Technology* **2017,** *313*, 1-8.

[f] See: http://www.freemantech.co.uk/_powders/powder-testing-bulk-properties

Table S4. Physical properties of test powders

Powder	Flow function coefficient	Bulk density (g/cc)	Tap density (g/cc)	True density (g/cc)	Particle size D[4,3] (μm)	Hygroscopic onset (RH%)	Hygroscopic maximum (%)	Hygroscopic final (%)	Morphology – SEM	Aspect ratio	Sphericity	Permeability (mBar)	Compressibility (%)
D-mannitol	4.8	0.573	0.815	1.4825	122	10%	0.15%	0%	laths	0.57	0.76	2.11	4.32
Fumed silica	4.1	0.0325	0.0481	2.3437	17.9	30%	27%	19%	agglomerated, irregular particles	0.71	0.73	10.10	23.05
L-proline	3.4	0.419	0.665	1.3698	94.6	50%	159%	19%	needles	0.45	0.71	0.90	2.21
Limestone powder	2.7	0.483	1.04	2.6798	4.23	50%	1%	0%	agglomerated, irregular particles	0.63	0.75	9.52	2.05
PVPP	6.0	0.343	0.458	1.2081	98.8	0%	44%	0%	agglomerated, irregular particles	0.72	0.81	1.95	2.77
Sodium chloride	>50	1.25	1.38	2.1543	348	60%	147%	0%	cubes	0.84	0.91	0.11	7.84
Thiamine HCl	6.5	0.241	0.448	1.3873	45.1	10%	35%	2.5%	plates	0.61	0.78	2.10	10.21

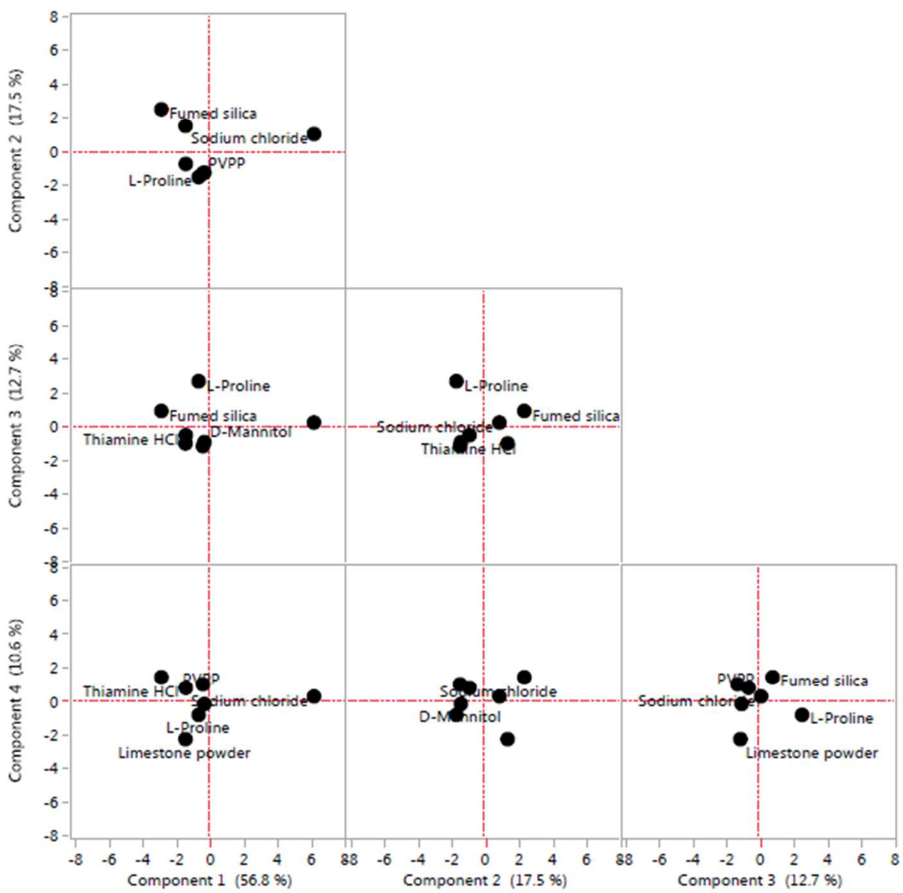
Table S5. SEM images of test powders

 D-Mannitol	 Fumed silica	 L-Proline
 Limestone powder	 PVPP	 Sodium chloride
 Thiamine HCl		

6. PCA summary plots and loading plot

A principal component analysis (PCA) was conducted on the physical property data in Table S4 to demonstrate that powders considered in the study spanned a wide range of physical properties.[g] The physical property data were described by four different components. The score plots of the physical properties of the powders are displayed in Figure 1 below.

Figure S4. Score plots of physical properties of powders based on four principal components



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[g] The PCA was performed in JMP ® Version 13.0.0, SAS Institute Inc., Cary, NC, 1989-2007. For the purposes of the PCA, a FFC value of 50 was used for sodium chloride.

7. Tables of discounted dispenses

Table S6. Chemspeed SWING discounted dispenses.

Machine stalls occurred most frequently with dispenses using D-mannitol (69), followed by thiamine HCl (14), PVPP (9), limestone powder (6) and L-proline (5). These machine stalls ended an intended run at varying points between run 1 dispense 1 and run 9 dispense 20, depending on which particular dispense experienced the machine stall. A machine stall occurring during an early dispense resulted in a larger number of subsequent zero value dispenses compared with a machine stall occurring during a later dispense. No machine stalls were observed for any of the 720 sodium chloride dispenses.

Equipment	Equipment Location	Company	Material	Target mass (mg)	Discounted from analysis			Retained for analysis	Dispenses attempted
					Machine stall	Questionable value	Zero value		
Chemspeed Swing	Purgebox	BMS	D-Mannitol	2			120	60	180
				10				180	180
				50	40		100	40	180
			L-Proline	2				120	120
				10	4		40	76	120
				50			60	60	120
			Limestone powder	2				120	120
				10				120	120
				50	6		40	74	120
			PVPP	2			60	120	180
				10	9		20	151	180
				50			120	60	180
			Sodium chloride	2				120	120
				10				120	120
				50				120	120
			Thiamine HCl	2			40	20	60
				10	14		20	26	60
				50			40	20	60
		Merck	D-Mannitol	2				60	60
				10			20	40	60
				50		1		59	60
			L-Proline	2			40	20	60
				10	1		41	18	60
				50			60		60
			PVPP	2				60	60
				10				60	60
				50				60	60
			Sodium chloride	2				60	60
				10				60	60
				50				60	60
			Thiamine HCl	2			40	20	60
				10			40	20	60
				50			59	1	60
		Pfizer	D-Mannitol	2			120	60	180
				10	10		80	90	180
				50	19		100	61	180
			PVPP	2				60	60
				10				60	60
				50				60	60
			Sodium chloride	2				60	60
				10				60	60
				50				60	60
Subtotal					103	1	1,260	2,776	4,140

Table S7. Mettler-Toledo Quantos QB5 discounted dispenses.

Four zero value dispenses were observed: two for sodium chloride in a fume cupboard environment and two for L-proline in a nitrogen purge box environment. Two questionable dispenses were observed: one for fumed silica in an LEV environment and one for sodium chloride in an LEV environment.

Equipment	Equipment Location	Company	Material	Target mass (mg)	Discounted from analysis		Retained for analysis	Dispenses attempted
					Questionable value	Zero value		
Mettler Toledo Quantos	Fume cupboard	AZ	D-Mannitol	2			40	40
				10			60	60
				50			40	40
			Limestone powder	2			60	60
				10			60	60
				50			60	60
			PVPP	2			60	60
				10			60	60
				50			60	60
			Sodium chloride	2			60	60
				10		1	59	60
				50		1	59	60
			Thiamine HCl	2			60	60
				10			60	60
				50			60	60
	Glovebox	AZ	D-Mannitol	2			60	60
				10			60	60
				50			60	60
			PVPP	2			60	60
				10			60	60
				50			60	60
	LEV	GSK	D-Mannitol	2			60	60
				10			60	60
				50			60	60
			Fumed silica	2			60	60
				10	1		59	60
			L-Proline	2			60	60
				10			60	60
				50			60	60
			Limestone powder	2			60	60
				10			60	60
				50			60	60
			PVPP	2			60	60
				10			60	60
				50			60	60
			Sodium chloride	2	1		59	60
				10			60	60
				50			60	60
			Thiamine HCl	2			60	60
				10			60	60
				50			60	60
	Purgebox	Pfizer	D-Mannitol	2			60	60
				10			60	60
				50			60	60
			Fumed silica	2			60	60
				10			60	60
			L-Proline	2		2	58	60
				10			60	60
				50			60	60
			Limestone powder	2			80	80
				10			80	80
				50			80	80
			PVPP	2			60	60
				10			60	60
				50			60	60
			Sodium chloride	2			60	60
				10			60	60
				50			60	60
			Thiamine HCl	2			60	60
				10			60	60
				50			78	78
Subtotal					2	4	3,692	3,698

Table S8. Unchained Labs Freeslate discounted dispenses.

152 machine time outs were observed: 99 for sodium chloride/glovebox, 50 for thiamine HCl/glovebox, 2 for thiamine HCl/open bench, 1 for PVPP/open bench. 43 zero value dispenses were observed: 26 for L-proline/glovebox, 15 for thiamine HCl/glovebox, 2 for PVPP/open bench. 15 questionable value dispenses were observed: 5 for D-mannitol/glovebox, 5 for L-proline/open bench, 4 for PVPP/open bench, and 1 for sodium chloride/open bench.

Equipment	Equipment Location	Company	Material	Target mass (mg)	Discounted from analysis			Retained for analysis	Dispenses attempted
					Machine time out	Questionable value	Zero value		
Unchained Labs Freeslate	Glovebox	AZ	D-Mannitol	2				60	60
				10		5		55	60
				50				60	60
			L-Proline	2			20	40	60
				10				60	60
				50			6	54	60
			Limestone powder	2				60	60
				10				60	60
				50				60	60
			PVPP	2				60	60
				10				60	60
				50				60	60
			Sodium chloride	2	53			7	60
				10	45			15	60
				50				60	60
			Thiamine HCl	2			15	45	60
				10	35			25	60
				50	15			45	60
	Open bench	BMS	D-Mannitol	2				120	120
				10				120	120
				50				120	120
			L-Proline	2				60	60
				10				60	60
				50		5		55	60
			Thiamine HCl	2				60	60
				10	2			58	60
				50				60	60
		Merck	D-Mannitol	2				60	60
				10				60	60
				50				60	60
			L-Proline	2				60	60
				10				60	60
				50				60	60
			PVPP	2				120	120
				10		4	2	114	120
				50	1			119	120
			Sodium chloride	2				60	60
				10		1		59	60
				50				60	60
			Thiamine HCl	2				120	120
				10				120	120
				50				120	120
	Glovebox	Pfizer	D-Mannitol	2				60	60
				10				60	60
				50				60	60
			L-Proline	2				60	60
				10				60	60
				50				60	60
			Limestone powder	2				60	60
				10				60	60
				50				60	60
			Sodium chloride	2				60	60
				10	1			59	60
				50				60	60
			Thiamine HCl	2				60	60
				10				60	60
				50				60	60
Subtotal					152	15	43	3,750	3,960

Table S9. Unchained Labs Junior discounted dispenses.

21 questionable value dispenses were observed: 16 for sodium chloride, 4 for D-mannitol and 1 for thiamine HCl. 20 zero value dispenses were observed for D-mannitol. One machine time out was observed for sodium chloride.

Equipment	Equipment Location	Company	Material	Target mass (mg)	Discounted from analysis			Retained for analysis	Dispenses attempted
					Machine Time Out	Questionable value	Zero value		
Unchained Labs Junior	LEV	GSK	D-Mannitol	2		2		438	440
				10		2		458	460
				50			20	440	460
			Fumed silica	2				120	120
				10				120	120
			L-Proline	2				120	120
				10				120	120
				50				120	120
			Limestone powder	2				180	180
				10				180	180
				50				180	180
			PVPP	2				240	240
				10				240	240
				50				240	240
			Sodium chloride	2	1	1		677	679
				10		4		696	700
				50		11		669	680
			Thiamine HCl	2				240	240
				10				240	240
				50		1		239	240
Subtotal					1	21	20	5,957	5,999

8. Tables of mean, median, %RSD dispense mass and dispense time data

Table S10. Chemspeed SWING mean, median, % RSD data

Platform	Environment	Powder	Dispense head	Target mass (mg)	# of Dispenses	Dispense mass data: Mean (mg)	Dispense mass data: Median (mg)	Dispense mass data: RSD (%)	# of Time values	Dispense time data: Mean (sec)	Dispense time data: Median (sec)	Dispense time data: RSD (%)
Chemspeed SWING	Purgebox	D-Mannitol	Type 1	10	60	10.88	10.8	5.52	0			
				50	24	50.35	50.3	1.10	0			
			Type 1D	2	60	2.24	2.2	14.68	0			
				10	120	10.31	10.2	3.39	0			
				50	16	50.31	50.1	0.99	0			
			Type 2	2	120	2.43	2.2	50.98	59	18.85	18	38.96
				10	130	10.78	10.2	13.85	40	48.00	47	12.71
				50	120	50.58	50.3	2.18	59	34.85	32	28.54
		Limestone powder	Type 1D	2	120	2.09	1.9	39.06	0			
				10	120	9.86	9.8	4.72	0			
				50	74	50.51	50.6	1.54	0			
		L-Proline	Type 2	2	20	2.24	2.0	43.02	19	17.53	17	15.95
				10	18	10.18	10.3	7.15	18	30.72	31	33.79
			Type 2D	2	60	2.89	2.9	14.79	0			
				10	60	10.55	10.5	3.52	0			
				50	60	50.43	50.3	0.86	0			
			Type 4	2	60	1.90	1.8	25.82	0			
				10	16	9.78	9.8	6.88	0			
		PVPP	Type 2	2	120	2.49	2.4	24.45	59	15.44	14	35.27
				10	120	10.44	10.3	5.77	60	21.30	20	26.74
				50	120	50.45	50.3	1.14	60	23.17	22	21.78
			Type 2D	2	120	2.32	2.2	15.71	0			
				10	151	10.27	10.1	3.77	0			
				50	60	50.39	50.4	0.35	0			
		Sodium chloride	Type 1	2	120	2.74	2.6	22.60	0			
				10	120	10.79	10.7	5.65	0			
				50	120	50.70	50.6	1.09	0			
			Type 2	2	120	2.41	2.3	27.52	59	21.10	17	46.20
				10	120	10.46	10.3	6.14	60	30.27	28	32.25
				50	120	50.83	50.5	2.11	60	19.50	16	44.10
		Thiamine HCl	Type 1	2	20	2.09	2.1	8.27	0			
				10	26	10.31	10.3	3.48	0			
				50	20	50.29	50.2	0.53	0			
			Type 2	2	20	2.33	2.5	17.45	19	16.53	16	10.93
				10	20	10.40	10.3	3.60	20	30.85	30	16.64
				50	1	44.80	44.8		1	53.00	53	
Total					2,776				593			

Table S11. Mettler-Toledo Quantos QB5 mean, median, %RSD data

Platform	Dispense head	Powder	Environment	Target mass (mg)	# of Dispenses	Dispense mass data Mean (mg)	Median (mg)	RSD (%)	# of Time values	Dispense time data Mean (sec)	Median (sec)	RSD (%)
Mettler Toledo Quantos	QH012-LNMP	D-Mannitol	Fume cupboard	2	40	2.35	2.23	10.22	0			
				10	60	10.59	10.39	4.52	0			
				50	40	50.46	50.41	0.54	0			
			Glovebox	2	60	2.07	2.02	6.48	0			
				10	60	9.84	9.82	1.14	0			
				50	60	48.46	48.44	0.42	0			
			LEV	2	60	2.08	2.06	3.90	60	24.48	24	50.49
				10	60	10.17	10.14	1.40	60	25.25	25	27.74
				50	60	50.51	50.45	0.50	60	28.02	28	13.87
			Purgebox	2	60	2.24	2.21	6.74	60	46.12	40	52.73
				10	60	10.41	10.37	1.55	60	32.45	32	16.84
				50	60	50.61	50.53	0.54	60	38.42	37	10.89
		Fumed silica	LEV	2	60	2.30	2.07	29.10	60	58.33	48	51.65
				10	59	10.55	10.50	2.44	59	86.00	85	28.07
			Purgebox	2	60	2.17	2.18	3.92	60	43.15	38	69.17
				10	60	10.52	10.52	0.85	60	49.35	49	7.13
		Limestone powder	Fume cupboard	2	60	2.11	2.10	1.63	0			
				10	60	10.20	10.15	1.67	0			
				50	60	50.17	50.15	0.17	0			
			LEV	2	60	2.12	2.09	4.73	60	26.92	24	61.73
				10	60	10.35	10.22	7.79	60	30.17	28	41.81
				50	60	50.58	50.35	1.32	60	38.90	37	26.60
			Purgebox	2	80	2.20	2.09	13.95	80	24.70	23	62.53
				10	80	10.22	10.20	1.75	80	25.38	24	28.14
				50	80	50.57	50.39	2.04	80	38.49	31	93.17
		L-Proline	LEV	2	60	2.07	2.07	1.54	60	30.33	30	26.06
				10	60	10.17	10.13	2.74	60	34.73	33	32.14
				50	60	50.32	50.26	0.61	60	44.87	44	29.02
			Purgebox	2	58	2.11	2.08	4.24	58	28.45	24	59.06
				10	60	10.14	10.15	1.86	60	30.43	29	27.52
				50	60	50.55	50.47	0.52	60	33.97	34	8.43
		PVPP	Fume cupboard	2	60	2.17	2.16	1.65	0			
				10	60	10.22	10.22	0.40	0			
				50	60	50.22	50.21	0.16	0			
			Glovebox	2	60	2.00	2.00	2.67	0			
				10	60	9.80	9.81	0.71	0			
				50	60	48.34	48.37	0.50	0			
			LEV	2	60	2.05	2.05	1.39	60	28.33	27	24.82
				10	60	10.15	10.16	0.24	60	29.97	30	15.33
				50	60	50.44	50.44	0.14	60	39.35	40	5.80
			Purgebox	2	60	2.09	2.07	3.70	60	36.90	29	74.09
				10	60	10.17	10.18	0.29	60	30.03	29	24.73
				50	60	50.37	50.37	0.13	60	38.63	40	9.68
		Sodium chloride	Fume cupboard	2	60	2.16	2.16	2.20	0			
				10	59	10.42	10.23	3.62	0			
				50	59	50.23	50.22	0.17	0			
			LEV	2	59	2.22	2.12	11.09	59	20.41	20	41.23
				10	60	11.36	10.28	39.75	60	18.05	18	18.65
				50	60	52.46	50.64	13.00	60	20.52	21	18.23
			Purgebox	2	60	2.16	2.12	9.63	60	21.57	21	33.78
				10	60	11.18	10.21	29.34	60	20.43	21	22.28
				50	60	50.79	50.60	2.03	60	21.47	21	13.33
		Thiamine HCl	Fume cupboard	2	60	2.09	2.11	13.15	0			
				10	60	10.18	10.15	0.98	0			
				50	60	50.18	50.16	0.14	0			
			LEV	2	60	2.06	2.06	1.36	60	31.23	29	45.31
				10	60	10.14	10.15	0.55	60	34.45	34	12.46
				50	60	50.42	50.43	0.18	60	37.58	38	6.76
			Purgebox	2	60	2.05	2.05	1.30	60	35.07	30	72.15
				10	60	10.12	10.13	0.38	60	35.02	34	22.07
				50	78	50.33	50.31	0.32	78	46.69	36	181.01
Total					3,692				2,474			

Table S12. Unchained Labs Freeslate mean, median, %RSD data

Platform	Environment	Powder	Dispense head	Target mass (mg)	# of Dispenses	Dispense mass data			# of Time values	Dispense time data		
						Mean (mg)	Median (mg)	RSD (%)		Mean (sec)	Median (sec)	RSD (%)
Unchained Labs Freeslate	Glovebox	D-Mannitol	SV	2	120	2.00	1.9	14.73	120	61.48	54	31.25
				10	115	10.00	9.9	6.86	115	95.03	74	41.99
				50	120	51.25	50.4	4.96	120	81.14	72	61.96
		Limestone powder		2	120	2.96	2.1	62.57	120	61.51	46	57.50
				10	120	11.09	10.5	14.47	120	93.83	57	70.94
				50	120	51.78	51.4	4.67	120	67.01	62	52.90
		L-Proline		2	100	1.97	1.9	24.02	100	79.54	74	48.34
				10	120	9.94	9.9	4.18	120	153.22	102	70.14
				50	114	50.91	50.2	3.08	114	106.52	88	55.89
		PVPP		2	60	1.71	1.8	10.10	60	334.78	114	127.29
				10	60	9.73	9.8	1.49	60	492.95	398	59.82
				50	60	49.81	49.8	0.31	60	222.38	180	60.86
		Sodium chloride		2	67	2.00	2.0	18.49	67	193.64	76	176.91
				10	74	10.43	10.2	7.83	74	152.92	66	173.52
				50	120	51.43	51.3	2.80	120	73.77	62	184.42
		Thiamine HCl		2	105	1.91	1.9	8.47	105	82.83	74	64.73
				10	85	10.05	10.0	3.26	85	211.41	82	142.37
				50	105	50.24	50.1	1.06	105	180.06	99	91.44
	Open Bench	D-Mannitol	Classic_plastic	2	60	3.87	2.1	90.77	60	109.85	124	59.06
				10	60	13.71	10.2	41.29	60	71.97	50	70.50
				50	60	50.36	50.0	2.10	60	110.48	104	48.16
			SV	2	120	2.10	2.0	12.02	120	50.41	45	32.77
				10	120	10.03	10.0	1.45	120	65.37	59	30.27
				50	120	50.10	50.0	0.69	120	66.58	64	34.63
		L-Proline	Classic_plastic	2	60	2.24	2.1	27.11	60	69.42	50	63.57
				10	60	10.28	10.1	6.56	60	83.45	63	52.07
				50	55	50.34	50.0	1.47	55	142.91	121	73.23
			SV	2	60	2.24	2.0	26.28	60	118.85	95	78.71
				10	60	11.03	10.6	14.71	60	103.15	62	112.07
				50	60	50.20	50.0	0.90	60	728.42	617	84.68
		PVPP	Classic_plastic	2	60	13.15	1.9	336.96	60	112.72	68	175.96
				10	54	17.62	10.1	84.27	54	115.06	74	110.34
				50	59	69.72	51.2	59.74	59	137.41	55	363.98
			SV	2	60	1.93	1.9	7.00	60	71.95	70	32.52
				10	60	9.99	10.0	1.54	60	57.38	51	28.09
				50	60	50.55	50.5	0.98	60	49.95	49	15.85
		Sodium chloride	SV	2	60	2.70	2.5	30.02	60	120.98	44	278.40
				10	59	11.76	11.0	17.86	59	92.58	52	108.03
				50	60	51.69	50.6	6.50	60	74.58	53	120.58
		Thiamine HCl	Classic_plastic	2	60	2.32	2.0	45.75	60	183.00	166	78.52
				10	60	10.53	10.4	5.77	60	165.28	136	59.85
				50	60	50.87	50.6	1.89	60	612.38	525	71.49
			SV	2	120	2.03	2.0	7.50	120	81.21	68	77.91
				10	118	10.04	10.0	1.87	118	131.36	69	142.20
				50	120	50.31	50.2	0.87	120	77.98	64	96.53
Total					3,750				3,750			

Table S13. Unchained Labs Junior mean, median, %RSD data

Platform	Environment	Powder	Dispense head	Target mass (mg)	# of Dispenses	Dispense mass data			# of Time values	Dispense time data		
						Mean (mg)	Median (mg)	RSD (%)		Mean (sec)	Median (sec)	RSD (%)
Unchained Labs Junior	LEV	D-Mannitol	Classic_metal	2	238	2.44	2.0	67.21	238	133.58	80	110.60
				10	238	10.46	10.1	13.31	238	56.70	48	74.02
				50	240	50.85	50.5	2.87	240	46.31	43	35.51
			Classic_plastic	2	60	2.04	2.0	4.95	60	114.62	86	95.24
				10	60	10.67	10.4	7.66	60	48.92	39	83.83
				50	60	52.44	52.0	4.44	60	49.60	40	69.27
			SV	2	140	3.24	2.0	127.22	140	71.81	51	120.72
				10	160	11.44	10.1	31.85	160	63.88	53	136.37
				50	140	52.37	50.7	8.17	140	79.14	46	145.39
		Fumed silica	Classic_metal	2	60	2.06	2.0	5.18	60	569.50	384	105.59
				10	60	10.16	10.1	1.77	60	126.72	88	82.61
			SV	2	60	2.15	2.0	13.36	60	115.78	71	124.08
				10	60	10.19	10.1	2.56	60	301.68	246	73.05
		Limestone powder	Classic_metal	2	120	2.46	2.2	40.62	120	139.07	79	150.05
				10	120	13.06	11.6	31.80	120	69.09	35	159.34
				50	120	53.69	52.3	7.75	120	57.03	51	54.97
			SV	2	60	2.20	2.1	10.03	60	59.33	49	60.74
				10	60	10.36	10.2	4.25	60	57.35	54	42.08
				50	60	51.08	50.8	2.10	60	46.53	44	33.46
		L-Proline	Classic_metal	2	60	2.87	2.3	46.95	60	46.30	28	105.21
				10	60	11.08	10.7	11.83	60	32.33	25	63.46
				50	60	51.15	50.9	1.51	60	50.38	49	21.14
			SV	2	60	2.06	2.0	5.50	60	64.57	73	44.10
				10	60	10.19	10.2	1.65	60	51.90	47	36.78
				50	60	50.71	50.6	1.51	60	95.80	53	321.45
		PVPP	Classic_metal	2	120	2.25	2.0	29.77	120	105.62	77	86.79
				10	120	10.37	10.1	7.49	120	50.62	47	46.26
				50	120	50.77	50.7	1.14	120	43.77	41	18.84
			Classic_plastic	2	60	2.07	2.0	10.40	60	75.00	67	42.63
				10	60	10.35	10.2	4.68	60	51.02	41	75.72
				50	60	53.25	51.2	12.87	60	42.12	40	34.54
			SV	2	60	2.07	2.0	4.79	60	98.68	78	112.68
				10	60	10.21	10.1	3.45	60	50.45	45	38.66
				50	60	50.85	50.6	1.76	60	70.42	47	164.42
		Sodium chloride	Classic_metal	2	537	3.49	2.1	129.05	537	68.18	36	121.14
				10	536	11.05	10.2	17.35	536	47.36	38	109.04
				50	530	64.03	51.4	82.33	530	43.58	37	73.92
			SV	2	140	4.29	3.1	73.12	140	62.70	27	138.18
				10	160	15.00	12.3	45.39	160	41.75	27	150.43
				50	139	59.46	56.2	16.31	139	45.99	32	163.62
		Thiamine HCl	Classic_metal	2	120	2.15	2.0	19.46	120	93.37	65	83.72
				10	120	10.13	10.1	1.96	120	52.27	47	52.62
				50	120	50.93	50.8	1.26	120	46.78	44	24.82
			Classic_plastic	2	60	2.26	2.2	12.68	60	171.08	69	120.66
				10	60	10.42	10.4	3.35	60	118.60	79	205.20
				50	59	50.89	50.8	1.53	59	364.39	286	89.94
			SV	2	60	2.05	2.0	3.76	60	58.72	56	34.34
				10	60	10.12	10.1	1.59	60	51.82	49	40.87
				50	60	50.67	50.6	1.01	60	56.92	50	36.81
Total					5,957				5,957			

9. Additional charts of % error vs. dispense time

Figure S5. % error vs. dispense time on Chemspeed SWING system. Scatterplot of % error values (-25% to +1000%) vs. dispense time (0 – 500 seconds), broken down by powder (columns) and target mass in mg (rows). All dispenses used a Type 2 dispense head. All dispenses were performed in a purgebox environment.

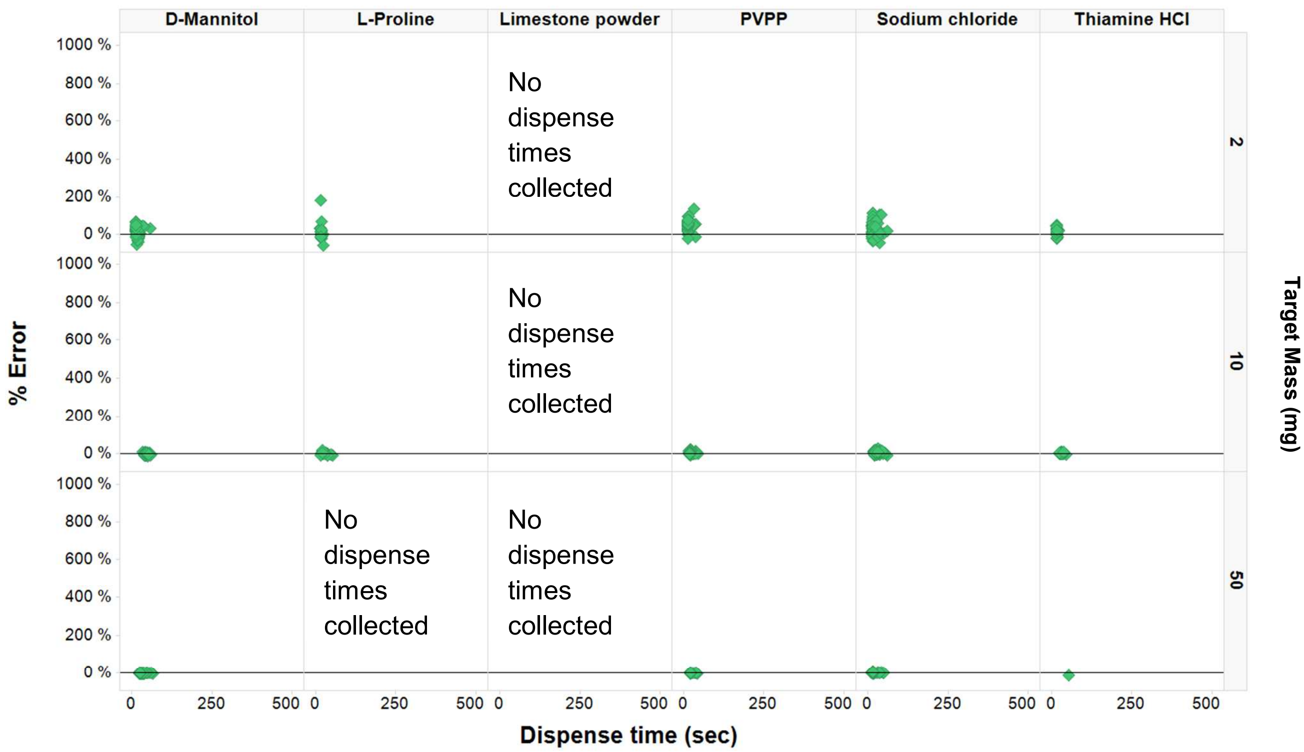


Figure S6. % error vs. dispense time on Mettler-Toledo Quantos QB5 systems. Scatterplot of % error values (-25% to +1000%) vs. dispense time (0 – 500 seconds), broken down by powder (columns), target mass in mg (rows), and equipment location (colors). All dispenses used a QH012-LNMP dispense head.

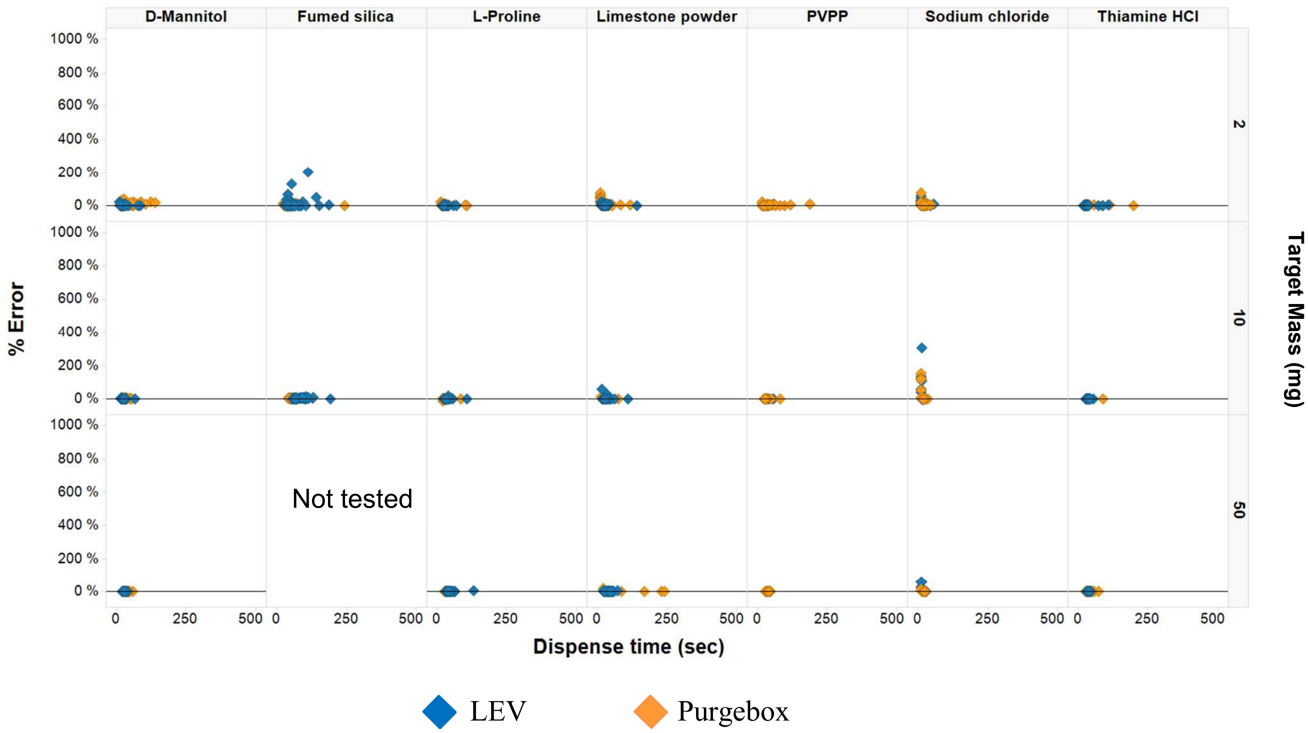


Figure S7. % error vs. dispense time on Unchained Labs Freeslate systems. Scatterplot of % error values (-25% to +1000%) vs. dispense time (0 – 500 seconds), broken down by powder (columns), target mass in mg (rows), and equipment location/dispense head (colors).

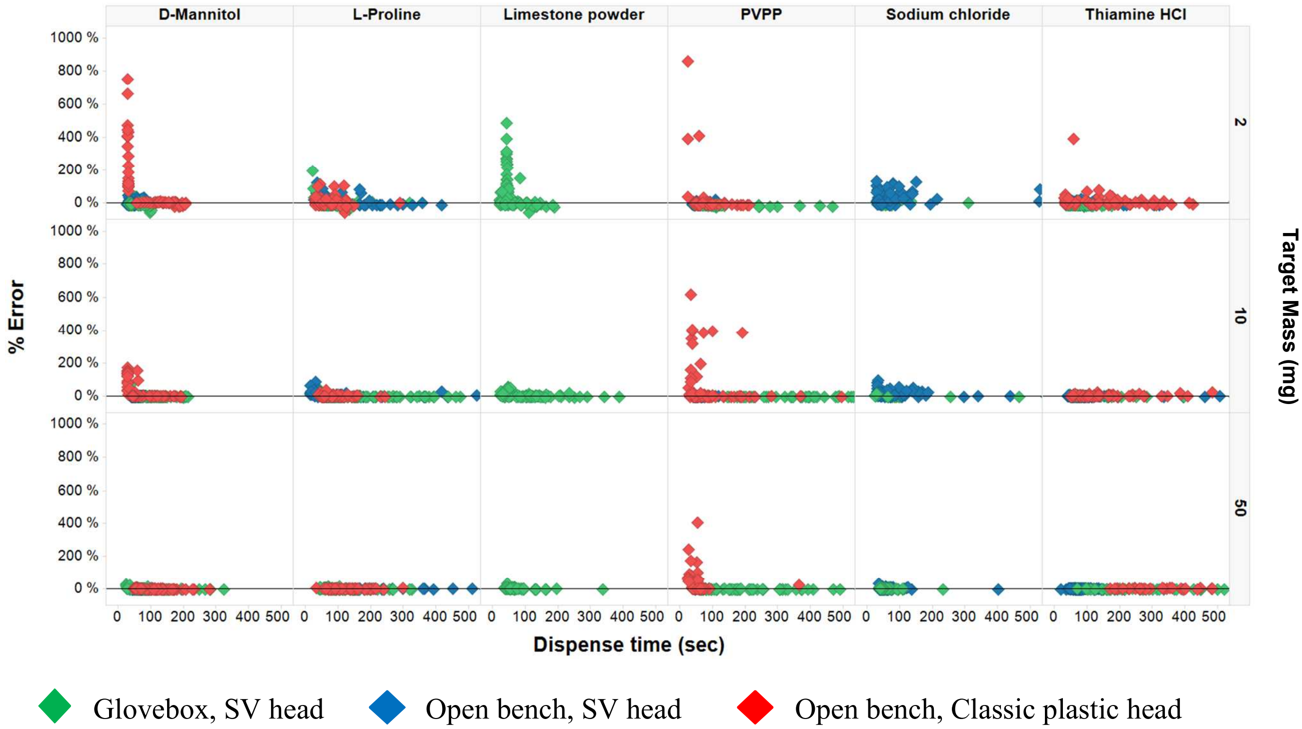
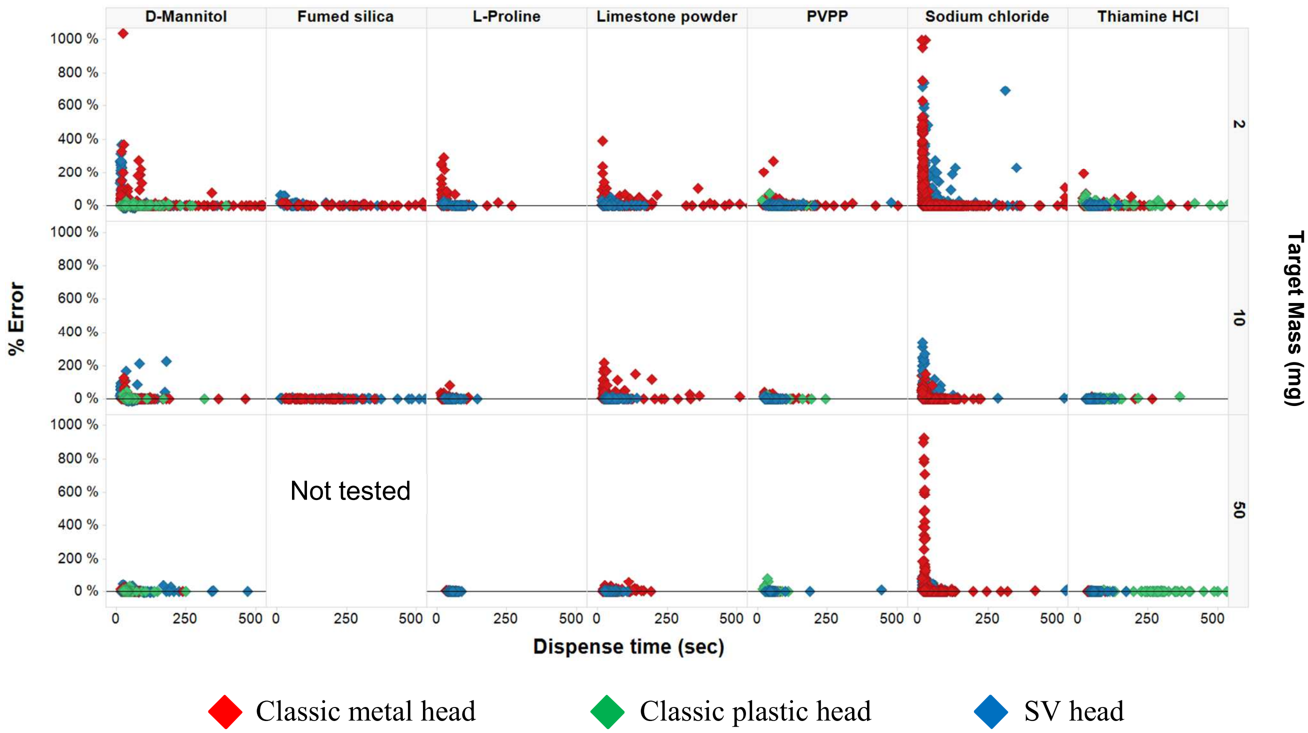


Figure S8. % error vs. dispense time on Unchained Labs Junior system. Scatterplot of % error values (-25% to +1000%) vs. dispense time (0 – 500 seconds), broken down by powder (columns), target mass in mg (rows), and dispense head (colors). All dispenses were performed in an LEV environment.



10. Additional data tables

Table S14. Mean mass and % RSD mass values from dispenses in purgebox environment

Powder	Target mass (mg)	Chemspeed SWING		Dispense head	Mettler-Toledo Quantos	
		Mean mass (mg)	RSD mass (%)		Mean mass (mg)	RSD mass (%)
D-Mannitol	2	2.24	14.68	Type 1D	2.24	6.74
D-Mannitol	10	10.31	3.39	Type 1D	10.41	1.55
D-Mannitol	50	50.31	0.99	Type 1D	50.61	0.54
Limestone powder	2	2.09	39.06	Type 1D	2.20	13.95
Limestone powder	10	9.86	4.72	Type 1D	10.22	1.75
Limestone powder	50	50.51	1.54	Type 1D	50.57	2.04
L-Proline	2	2.24	43.02	Type 2	2.11	4.24
L-Proline	10	10.18	7.15	Type 2	10.14	1.86
L-Proline	50	50.43	0.86	Type 2D	50.55	0.52
PVPP	2	2.32	15.71	Type 2D	2.09	3.70
PVPP	10	10.27	3.77	Type 2D	10.17	0.29
PVPP	50	50.39	0.35	Type 2D	50.37	0.13
Sodium chloride	2	2.41	27.52	Type 2	2.16	9.63
Sodium chloride	10	10.46	6.14	Type 2	11.18	29.34
Sodium chloride	50	50.70	1.09	Type 1	50.79	2.03
Thiamine HCl	2	2.09	8.27	Type 1	2.05	1.30
Thiamine HCl	10	10.31	3.48	Type 1	10.12	0.38
Thiamine HCl	50	50.29	0.53	Type 1	50.33	0.32

Table S15. Mean mass and % RSD mass values from dispenses in LEV environment

Powder	Target mass (mg)	Mettler-Toledo Quantos		Unchained Labs Junior		
		Mean mass (mg)	RSD mass (%)	Mean mass (mg)	RSD mass (%)	Dispense head
D-Mannitol	2	2.08	3.90	2.04	4.95	classic plastic
D-Mannitol	10	10.17	1.40	10.67	7.66	classic plastic
D-Mannitol	50	50.51	0.50	50.85	2.87	classic metal
Fumed silica	2	2.30	29.10	2.06	5.18	classic metal
Fumed silica	10	10.55	2.44	10.16	1.77	classic metal
Limestone powder	2	2.12	4.73	2.20	10.03	SV
Limestone powder	10	10.35	7.79	10.36	4.25	SV
Limestone powder	50	50.58	1.32	51.08	2.10	SV
L-Proline	2	2.07	1.54	2.06	5.50	SV
L-Proline	10	10.17	2.74	10.19	1.65	SV
L-Proline	50	50.32	0.61	50.71	1.51	SV
PVPP	2	2.05	1.39	2.07	4.79	SV
PVPP	10	10.15	0.24	10.21	3.45	SV
PVPP	50	50.44	0.14	50.77	1.14	classic metal
Sodium chloride	2	2.22	11.09	3.49	129.05	classic metal
Sodium chloride	10	11.36	39.75	11.05	17.35	classic metal
Sodium chloride	50	52.46	13.00	59.46	16.31	SV
Thiamine HCl	2	2.06	1.36	2.05	3.76	SV
Thiamine HCl	10	10.14	0.55	10.12	1.59	SV
Thiamine HCl	50	50.42	0.18	50.67	1.01	SV