

Assessment of Accuracy and Precision of Four Methods of Monitoring In-Use Volume of Multi-Dose Controlled Substance Vials

Lauren Forsythe, PharmD, DICVP, FSVHP, Jessica Barazowski, PharmD, FSVHP

Department of Veterinary Clinical Medicine, College of Veterinary Medicine, University of Illinois at Urbana-Champaign

INTRODUCTION

- Controlled substances must be closely tracked to monitor for diversion.
- An ideal method of tracking inventory for in-use multi-dose vials is not specified in Federal regulation.
- Methods commonly considered in veterinary medicine include:
 - Weight tracking (weighing the dose withdrawn or weighing the contents remaining in the vial)
 - Periodic actual draws of the remaining volume to compare to expected volume
 - Tracking total discrepancy amount at the end of each vial as a percentage of the starting volume
 - Using manufacturer or homemade vial markers to visually estimate volume remaining
- Questions frequently arise about the validity of each method and the appropriate use cases in practice.

AIM

Evaluate the accuracy and precision of each of the 4 methods described above.

CONCLUSIONS

Weight Tracking

- Accuracy and precision of weight tracking increases with increasing volume/dose. Therefore, this method is best for drugs that are using amounts greater than a 0.5 mL/dose.
- Weight tracking accuracy and precision were only dependent on scale for vial weights.
- Dose weight in syringe and weight of volume remaining provide comparable accuracy and precision.

Actual Draws

- Actual hub loss converged on 0.04 mL regardless of whether starting volume included overfill.

Discrepancy Percentage per Vial

- Percentage discrepancy per vial can provide trend tracking based on normal distribution principles.

Visual Inspection

- Based on calculations used, direct comparison to other methods by percentage is difficult. However, the wide spread of volume differences show this method is less ideal than other methods.

Overall

- Either vial weights or actual draws should be used and supplemented with the other methods.

METHOD

Weight Tracking

- An empty sterile vial was pre-filled with 10 mL sterile water for injection
- Doses were removed to mimic typical use. The syringe with needle was weighed immediately prior to each draw and reweighed after the draw. The vial was weighed after each draw.
- The weights were recorded on two scales with differing readability.
- Actual weight in g/mL was calculated and compared to the expected weight of 1 g/mL.



Left: Mettler Toledo model XS105DU with Max 120 g and d= 0.01mg (Scale 1)

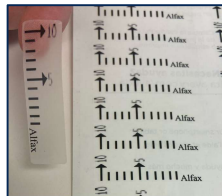


Right: Adventurer Pro AV812C with Max 810 g and d= 0.01g (Scale 2)

Dose Volume Summary Statistics	
Mean	0.20
Median	0.14
Min	0.01
Max	0.90
Count	33

Visual Inspection

- In conjunction with the weight tracking, visual inspection was completed between each dose removal. Estimated amount remaining was recorded.
- A homemade volume marker was affixed to the side of the vial assuming a volume of 10 mL at the start to aid in visual inspection.



Left: Homemade volume markers.



Right: Vial with a homemade volume marker.

Actual Draws

- An empty sterile vial was pre-filled with 10.5 mL sterile water for injection
- Doses were removed to mimic typical use. After each dose was removed, the remaining quantity was withdrawn to determine amount remaining.
- Expected hub loss was calculated as 0.05 mL/stick. Actual hub loss was determined based on volume remaining.
- Calculations were completed based on the 10.5 mL start volume as well as the 10 mL start volume to more closely mimic typical conditions.

Discrepancy Percentages

- Total discrepancy volume per vial was determined for each methadone vial from January 2022 through March 2023 (n=82).
- Discrepancy percentage was calculated based on a 10 mL fill volume.

Results - Weight Tracking

Precision

The amount of deviation of g/mL weight for each measurement compared to the mean g/mL weight.

Accuracy

The amount of deviation of g/mL weight for each measurement compared to 1 g/mL (density of water).

Table: Summary Data for Accuracy and Precision of Weight Tracking

	Scale 1				Scale 2			
	Accuracy		Precision		Accuracy		Precision	
Syringe	Vial	Syringe	Vial	Syringe	Vial	Syringe	Vial	
Mean (%)	52.90	13.57	75.72	62.49	51.56	14.18	76.36	63.03
Median (%)	68.39	48.24	86.18	78.36	66.67	50.00	86.28	77.83
Min (%)	-7062.10	-7206.60	-181.43	-294.67	-3009.00	-7009.00	-137.60	-284.92
Max (%)	97.75	97.46	96.08	92.89	97.78	97.78	98.21	94.29
Spread (%)	469.85	818.06	277.51	387.57	397.78	797.78	235.81	379.21

Table: Effect of Volume on Accuracy and Precision (linear regression analysis)

	Scale 1				Scale 2			
	Accuracy		Precision		Accuracy		Precision	
Syringe	Vial	Syringe	Vial	Syringe	Vial	Syringe	Vial	
R ²	0.14	0.14	0.01	0.01	0.16	0.14	0.01	0.01
P-value	0.03*	0.03*	0.55	0.55	0.02*	0.03*	0.65	0.55

Table: Summary Data for Difference Between Scales

	Difference Between Scales	
	Syringe	Vial
Mean (%)	0.01	0.01
Median (%)	0.02	0.03
Min (%)	0.00	0.00
Max (%)	0.62	0.21
Spread (%)	0.62	0.20

Table: Syringe vs Vial Accuracy and Precision (t-test; two-sided)

	Scale 1		Scale 2	
	Accuracy	Precision	Accuracy	Precision
P-value	0.18	0.36	0.34	0.32

Table: Effect of Volume on Difference Between Scales (linear regression analysis)

	Difference Between Scales	
	Syringe	Vial
R ²	0.32	0.44
P-value	0.07	0.01*

Table: Example variation across equal volume measurements.

Volume (mL)	Mean (g/mL)*	Spread (g/mL)*	Sample Count
0.11	1.40	0.04	3
0.12	1.38	0.03	6
0.14	1.32	0.05	4
0.15	1.45	0.03	6

Table: Accuracy and precision percentages by method

	Dose Weight- Syringe (Scale 1)		Dose Weight- Vial (Scale 1)		Dose Weight- Syringe (Scale 2)		Dose Weight- Vial (Scale 2)	
	Accuracy	Precision	Accuracy	Precision	Accuracy	Precision	Accuracy	Precision
Median (%)	68.39	86.18	48.24	78.36	66.67	86.28	50	77.83

Results - Visual Inspection

Precision

The amount of deviation of accuracy percentage for each measurement compared to the mean accuracy percentage.

Accuracy

The amount of deviation in mL for each visual observation compared to the actual volume remaining.

Table: Summary Data for Accuracy and Precision of Visual Inspection

	Marked as 10 mL Start Volume			
	Accuracy		Precision	
Mean (%)	84.45	92.26	92.26	92.26
Median (%)	86.79	95.72	95.72	95.72
Min (%)	75.00	84.62	84.62	84.62
Max (%)	97	99.80	99.80	99.80
Spread (%)	22.44	15.18	15.18	15.18

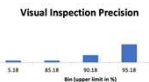
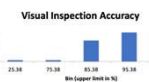


Table: Effect of Volume on Accuracy and Precision of Visual Inspection (linear regression analysis)

	10 mL Start Volume	
	Accuracy	Precision
R ²	0.01	0.01
P-value	0.69	0.69



Results - Actual Draws

Precision

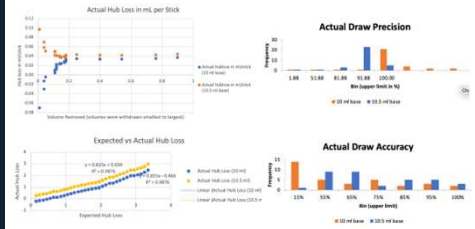
The amount of deviation of hub loss in mL/stick for each actual draw compared to the mean hub loss in mL/stick.

Accuracy

The amount of deviation of actual hub loss in mL/stick for each actual draw compared to an expected hub loss of 0.05 mL/stick.

Table: Summary Data for Accuracy and Precision of Actual Draws

	10 mL start volume		10.5 mL start volume	
	Accuracy	Precision	Accuracy	Precision
Mean (%)	22	18.52	67	83.86
Median (%)	13	21.61	63	88.70
Min (%)	-1	-136.83	49	-8.12
Max (%)	64	793.97	1000	95.76
Spread (%)	65	206.99	51	103.87



Results - Discrepancy Percentages

Precision

The amount of deviation of discrepancy percentage for each measurement compared to the mean discrepancy percentage.

Accuracy

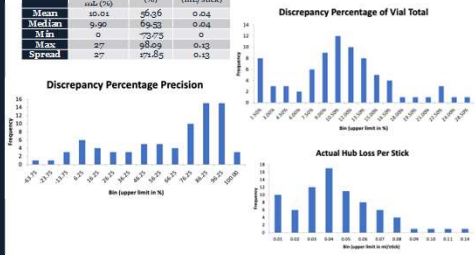
Not applicable

Table: Summary Data for Precision of Percent Discrepancies

	Marked as 10 mL Start Volume	
	Discrepancy Percent of Total (%)	Hub Loss (mL/stick)
Mean	10.01	0.04
Median	9.90	0.04
Min	0	-77.73
Max	27	99.89
Spread	27	97.85

Table: Effect of Number of Sticks on Precision of Total Discrepancy (linear regression analysis)

	10 mL start volume	
	Accuracy	Precision
R ²	0.01	0.04
P-value	0.94	0.34



Results - Comparison of Methods

	Weight Tracking*		Actual Draws*		Discrepancy % of Total		Visual Inspection*	
	Accuracy	Precision	Accuracy	Precision	Accuracy	Precision	Accuracy	Precision
Median (%)	58.33	82.16	38	55.16	N/A	69.53	86.79	95.72

*Visual inspection data is based on larger volumes which limits comparability to other methods

*Average of accuracy and precision means

