

ACCURACY AND PRECISION STUDY OF TOPICAL DISPENSERS

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OBJECTIVE

To study the precision and accuracy of dispensing devices used for veterinary compounds that are capable of measuring minute doses (~1/10th mL) of cream or gel preparations. The amount of cream dispensed among three devices—TICKERmini™, AccuPen™, and 1 mL syringe—was analyzed to establish each device's accuracy and precision.

EXPERIMENTAL

Materials

- 1 mL Syringe x 45
- TICKERmini™ x 3
- 7.5 mL AccuPen™ x 6
- PCCA Lipoderm® cream
- Ohaus Adventurer AX224 AutoCal balance
- Plastic Square Weigh Boats
- 100 mL Unguator Jar
- Spatula

Overview

Three trials with each device—TICKERmini™, 2-7.5 mL AccuPens™, and 15-1mL syringes— were performed. Each device was filled with PCCA Lipoderm® and two actuations of the TICKERmini™, one actuation of the AccuPen™, and 1 push equaling 0.1 mL of the 1 mL syringes were performed. The volume of each output of cream was recorded.

The cream used in each device was PCCA Lipoderm®. Upon research, it was shown that Lipoderm® cream was most prevalently used in veterinary products.

The balance used for the entire study was an Ohaus Adventurer AX224 AutoCal. The level bubble was centered in the circle, indicating that the balance was leveled.

Methodology

The weight of each empty device/group of devices was attained. Each device was filled with PCCA Lipoderm® to its maximum capacity and, with an exception of the syringes, tapped every quarter of the way to reduce and eliminate air bubbles. Each syringe was tapped after filling completely. The devices were allowed to sit at least 24 hours for the cream to settle, but did not exceed 36 hours.

Each device was primed > 24 hours after filling. Priming for each device was as followed:

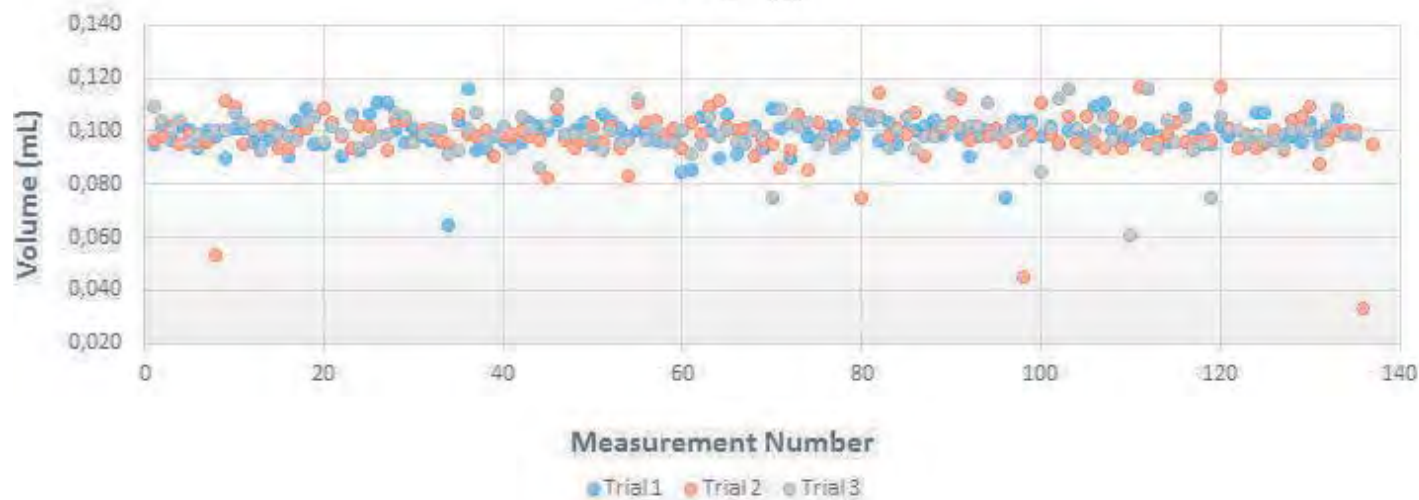
- Syringe: cream was expelled with the plunger up to the "1 mL" mark
- TICKERmini™: device was clicked until 15 grams of cream remained
- AccuPen™: device was pumped until 7.5 grams of cream remained in each device

The weight of each device with cream was recorded, and the weight of the cream was determined. To measure the amount of cream expelled from each device, one actuation* was performed. Using a timer, the cream was then allowed to fully accumulate for 10 seconds prior to harvesting the cream onto a weigh boat. The straight edge of the weigh boat was used to fully scrape the cream off the tip of each apparatus. The weight of the weigh boat + cream was "tared" at each step, and the weight of cream per actuation was recorded. This was repeated until all cream was dispensed, then the weights of the residual cream in the devices were recorded.

*Actuation definition

- Syringe = 0.1 mL push
- TICKERmini™ = 2 clicks
- AccuPen™ = 1 pump

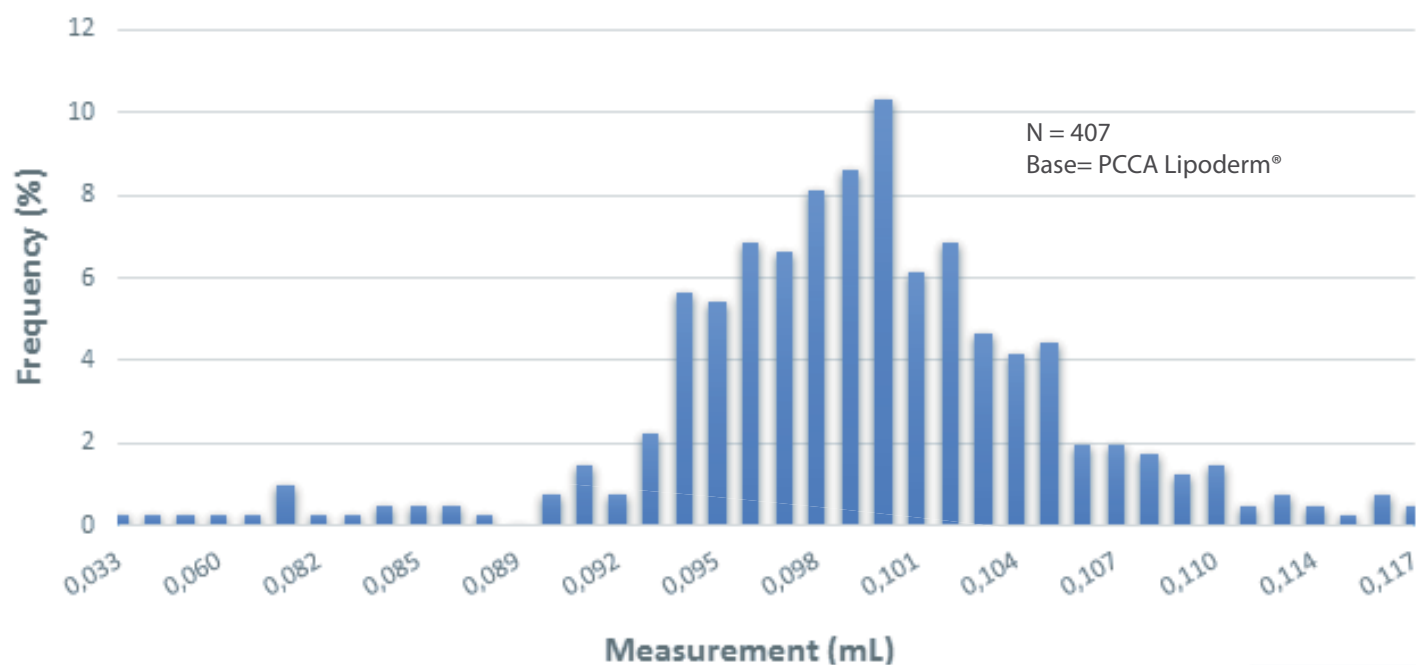
Accuracy and Precision 1 mL Syringe



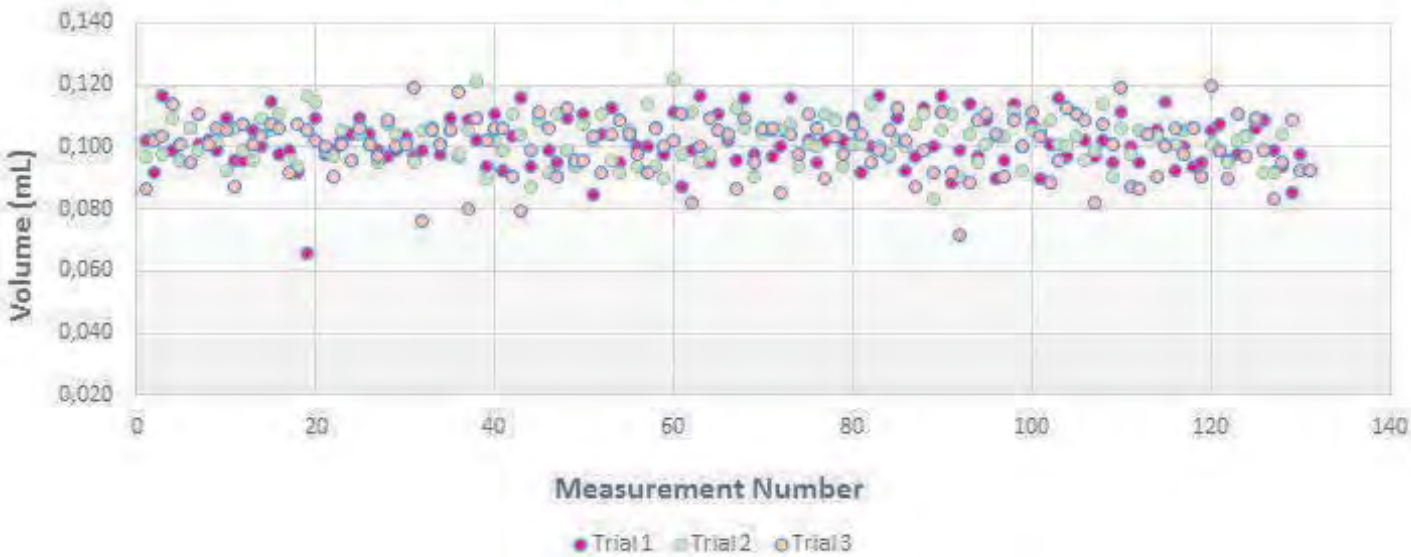
* Target = 0.1 mL

	Sample Size	Mean Volume of Cream/0.1-mL push	Median Volume of Cream/ 0.1-mL push	Standard Deviation	*Target Percentage	Volume of Cream/15 mL	Residual/15 mL	Time to Load
Trial 1	135	0.099 mL	0.099 mL	0.006 mL	99.084	15.095 mL	0.886 mL	9:33
Trial 2	137	0.098 mL	0.099 mL	0.010 mL	98.107	14.800 mL	0.864 mL	6:52
Trial 3	135	0.099 mL	0.100 mL	0.007 mL	99.452	15.004 mL	0.884 mL	4:53
Average		0.099 mL	0.099 mL	0.008 mL	98.881	14.966 mL	0.878 mL	7:06

Measurement Frequency 1 mL Syringe



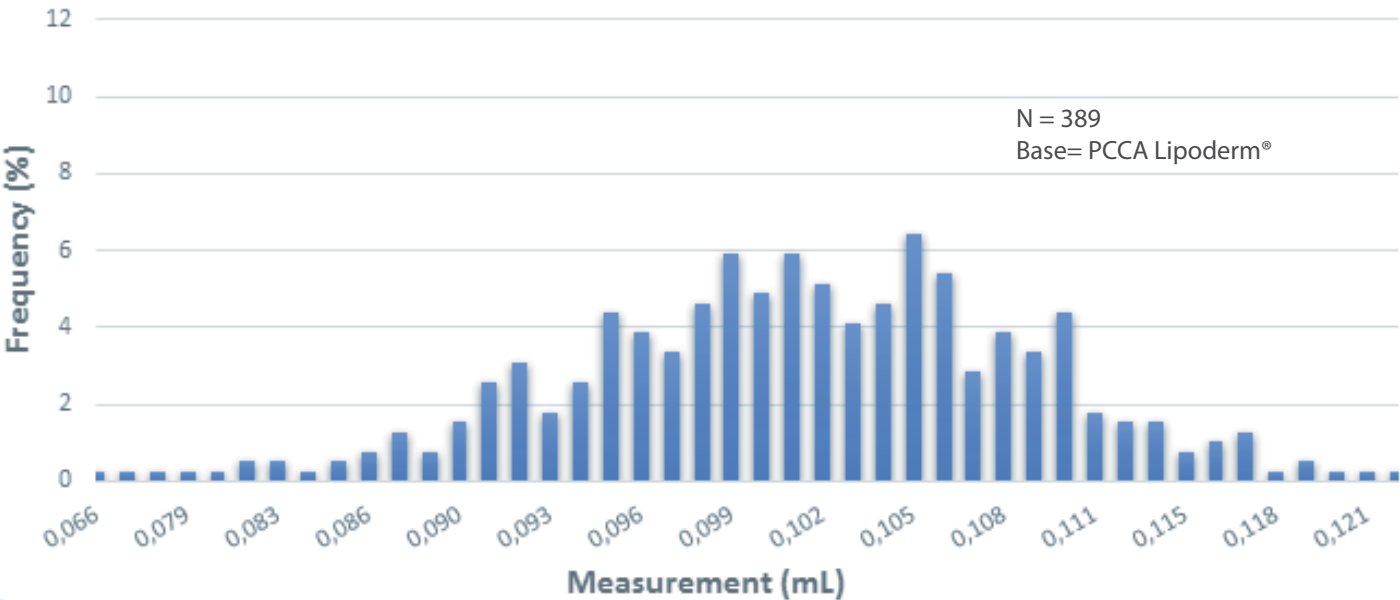
Accuracy and Precision
TICKERmini™



	Sample Size	Mean Volume of Cream/*2 Clicks	Median Volume of Cream/*2 Clicks	Standard Deviation	**Target Percentage	Volume of Cream/ TICKERmini™	Residual Volume/ TICKERmini™	Time to Load
Trial 1	130	0.102 mL	0.100 mL	0.008 mL	101.506	15.688 mL	2.058 mL	1:22
Trial 2	128	0.102 mL	0.102 mL	0.007 mL	101.856	15.668 mL	1.956 mL	1:04
Trial 3	131	0.101 mL	0.102 mL	0.009 mL	100.501	15.675 mL	1.968 mL	1:31
Average		0.101 mL	0.101 mL	0.008 mL	101.288	15.677 mL	1.994 mL	1:19

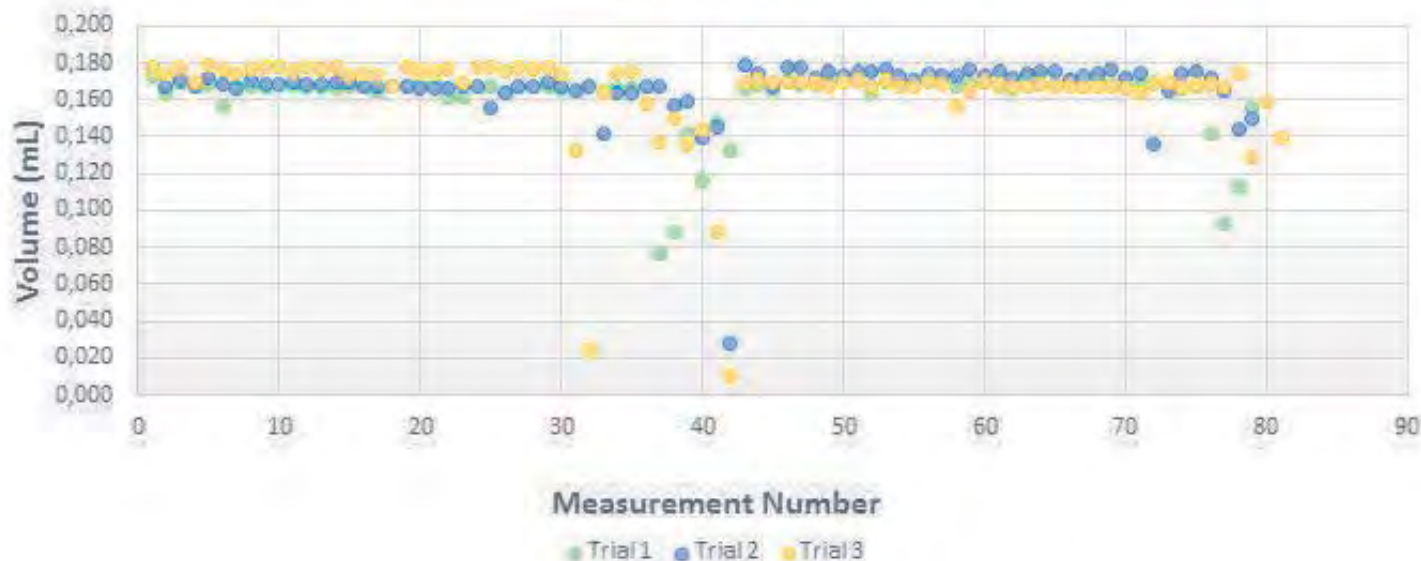
**Target = 0.1 mL/ 2 clicks

Measurement Frequency
TICKERmini™



Accuracy and Precision

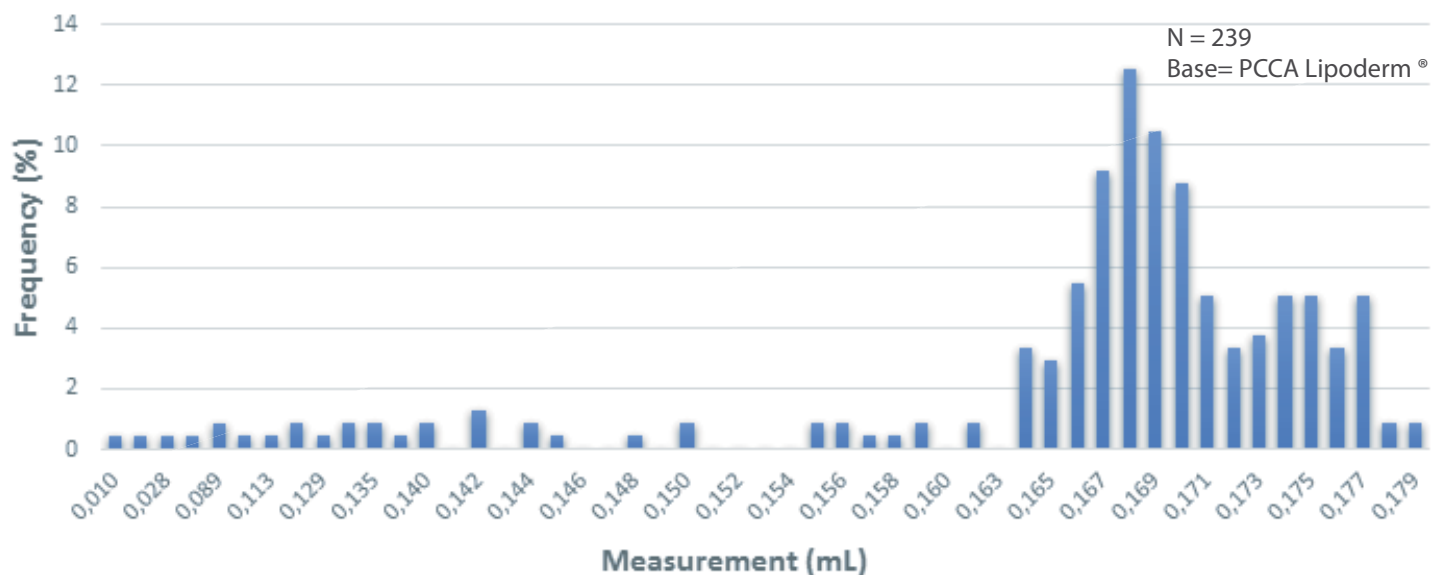
AccuPen™



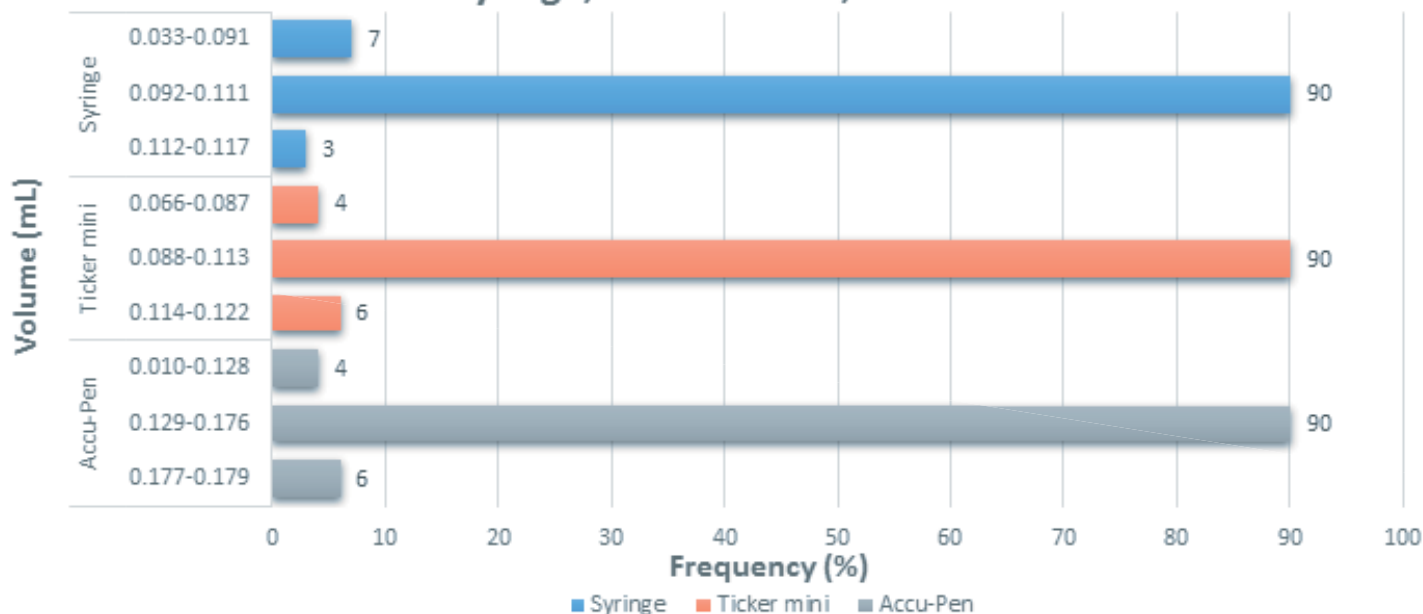
	Sample Size	Mean Volume of Cream/ Pump	Median Volume of Cream/ Pump	Standard Deviation	*Target Percentage	Volume of Cream/2 AccuPens™	Residual Volume/2 AccuPens™	Time to Load
Trial 1	79	0.162 mL	0.168 mL	0.018 mL	129.283	15.659 mL	1.927 mL	4:06
Trial 2	79	0.166 mL	0.169 mL	0.018 mL	132.880	15.956 mL	1.684 mL	2:26
Trial 3	81	0.163 mL	0.170 mL	0.027 mL	130.669	15.892 mL	1.945 mL	1:32
Average		0.164 mL	0.169 mL	0.021 mL	130.944	15.836 mL	1.852 mL	2:41

Measurement Frequency

AccuPen™



Volume-Frequency Syringe, TICKERmini™, AccuPen™



DISCUSSION

This accuracy and precision study was conducted to determine the reliability of devices used to dispense minute dosages of cream. In particular, three devices commonly used in compounding pharmacies to dispense ~0.100 - 0.125 mL of cream were tested using a commonly used base—PCCA Lipoderm®. The corresponding number of devices were used to accommodate 15 grams of cream in each trial (ie. 15-1mL syringes, 1 TICKERmini™, and 2-7.5mL AccuPens™). The weight of the cream expelled was converted to volume using the specific gravity of PCCA Lipoderm® 0.96, per manufacturer listing. In contrast to other studies evaluating dose accuracies of various delivery systems such as the SoloSTAR and FlexPen at different doses, a single dose of 0.1 mL for the syringe and TICKERmini™ and 0.125 mL for the AccuPen™ was chosen due to the relevance of this dose for veterinary compounds such as methimazole, amitriptyline, atenolol, etc.

Of note, while conducting the study, 10 seconds were allowed for the cream to fully accumulate following each actuation prior to harvesting and weighing the dispensed amount. Ten seconds was determined to mimic a reasonable length of time for a patient to wait prior to applying cream after actuation, all the while collecting the maximum amount per actuation. The uniformity of the length of between actuation and harvesting is pertinent in comparing the different devices, in order to reduce the number of variables.



Syringe

With careful experimentation, it was found that the 1 mL syringe had an average accuracy of 98.881% and a precision of ± 0.008 mL. The average residual volume of cream found per 15 syringes was 0.878 mL. This volume was attained by calculating the average weight of cream remaining in each 1 mL syringe and calculating the average residual in each of the three trials. The mean of each trial's average was then attained and converted to volume using the specific gravity of the cream. The experiment provided excellent results; however, the preparation of 15 grams of cream was cumbersome; on average, the time spent to load 15-1 mL syringes was 7:06.

Upon measuring each 0.1 push, the weight of the cream expelled was attained. Of note, significant air bubbles were present in the 8th or 9th measurement of each syringe, resulting in cream weighing between 0.000 and 0.078 mL. Consequently, a cut-off weight of 0.080 mL was established to distinguish between cream and air bubbles in the 8th or 9th measurement. The single smallest measurement ≤ 0.080 mL in each syringe was discarded so that measurements containing large air bubbles were omitted.

In this study, the TICKERmini™ revealed an accuracy of 101.288% with a precision of ± 0.008 mL. The average residual amount of cream in each TICKERmini™ was 1.994 mL. The device required less time to load 15 g of cream, necessitating 1:19 per TICKERmini™.

With each click delivering ~ 0.05 mL, two clicks were performed for each measurement to attain a target of 0.1 mL. Notably, at the end of each trial, the values decreased as the last amounts of cream were dispensed. Similarly with the syringes, the actuations resembling large air bubbles at the end of each trial were omitted. The same cut-off weight of 0.080 mL ($\leq 80\%$ of the target value) was used, discarding the last values of each TICKERmini™ ≤ 0.080 mL. In trial 1, the last 6 values were removed; in trial 2, the last 7; in trial 3, the last 5. These values represented the minute amounts shortly before the dispenser discharged the last amount of cream.

AccuPen™

The study was initially designed to use the 15 mL AccuPen™; however, it was not as readily available. Instead, 2-7.5mL AccuPens™ were used to allow for a comparable volume of cream to be dispensed.

After reading various studies regarding the AccuPen™, it was revealed that it was designed to discharge 0.25 mL per two actuations; therefore a reference target of 0.125 mL per actuation was determined. This target falls in the range of 0.12 – 0.14 mL per actuation that the manufacturer proposes. With a target of 0.125 mL/actuation, the average accuracy of the AccuPen™ was 130.944% with a precision of ± 0.021 mL.

The average residual cream per two AccuPens™ was 1.852 mL, requiring 2:41 to load two AccuPens™. The average residual volume of cream was attained in the same fashion as with the syringe. The average residual of each trial was calculated and the three values were used to find the mean residual weight and converted to volume using the specific gravity of the cream.

One pump of cream was expelled and measured for comparison to the proposed 0.125 mL measurement. After collecting the data for each trial, the values resembling the last amounts of cream in each AccuPen™ were discarded. As with the syringe and TICKERmini™, the cut-off value was determined as 80% of the target value. In this case, the cut-off value was $0.80 * 0.125 \text{ mL} = 0.1 \text{ mL}$.

Of significance, two out of the six AccuPens™ evaluated jammed in the midst of the trials. While jammed, the devices required 9 and 13 pumps dispensing little to no cream until the AccuPen™ began dispensing regular amounts. These values were removed from the study, consequently, the results of the trials reflected more ideal conditions than were present.

The standard of deviation for the AccuPen™ study was much larger in comparison to the syringe and TICKERmini™. This larger variation could have been attributed to the smaller sample size in the AccuPen™ group, due to larger volumes per actuation.

After conducting this study, it was found that the 1 mL syringe and TICKERmini™ dispensed creams with accuracy to its proposed volume and with miniscule deviations. Conversely, the AccuPen™ dispensed volumes well over the manufacturer's suggested target, along with large deviations.

The results with the syringe were almost impeccable; however, accuracy and precision of the device was solely dependent on the operator. This attribute holds advantageous in that the amount dispensed can be very close to the target amount with much diligence. Yet, this can serve as a downfall in that the accuracy of the device is limited to the operator's skills.

On the other hand, the accuracy and precisions of the TICKERmini™ and AccuPen™ were attributed solely to the mechanics of the applicators. Operator skill, or lack of, was irrelevant to achieving the desired dose.



CONCLUSION AND APPLICABILITY

There are currently few delivery systems that dispense minute volumes of cream with accuracy. Dispensing small, accurate volumes of cream is most relevant in dosing veterinary medications, in which a common dose is 0.1 mL of medicated cream. The purpose of this study was to analyze the devices that are on the market used to dispense this quantity. The accuracy and precision of the 1 mL syringe, TICKERmini™, and AccuPen™ were evaluated to determine their reliability in accordance with their proposed volume dispensed.

The syringe and TICKERmini™ performed with accuracy and precision, while the AccuPen™ delivered inaccurate volumes with much variance.

As secondary endpoints, the amount of time to load each device and the residual volumes were evaluated. In order to dispense 15 g of PCCA Lipoderm® cream, 15-1 mL syringes were required, demanding ample time to prepare. With the TICKERmini™'s ability to dispense a larger quantity of cream, only one device was required to dispense 15 g of cream, allowing for rapid preparation. The AccuPen™ also required less time to prepare; however, the capacity was smaller than that of the TICKERmini™. The time saved in preparing compounds can be valuable in compounding pharmacies dispensing large prescription volumes. With regards to the residual volume, the syringe has far less residual amount when dispensing 15 g of cream, followed by the AccuPen™, then TICKERmini™. Smaller residual volume results in less unused cream.

In summary, the 1 mL syringe and TICKERmini™ provide accurate and precise doses of small volumes of cream, making these delivery systems more ideal for preparations including veterinary compounds. However, the performance of the syringe was operator-driven, while the TICKERmini™ was mechanics/piston-driven. A piston-driven apparatus is more likely to show performance continuity than that of an operator-driven device.

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