Accuracy and precision of Pulse Micro-dose Injection Device using Draxxin™, Excede®, Excenel® and sterile water

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Objectives

The use of traditional syringes with needles for treating pigs can pose a safety hazard to the animal and the food supply. Needles can cause damage to carcasses at the injection site,[1, 2, 4] be a hazard if they break while injecting[5], and can act as a fomite to spread disease.[3] These risks represent not only a pork safety concern, but they also have a significant economic impact on the pork industry. Abscesses and injection-site lesions alone cost the industry almost $1.5 million in 1994, according to the Pork Chain Quality Audit.[2] Needle-free injection devices address some of these issues. When using a needle-free injection device, it is important to know if the desired amount of product is truly being injected into the animal and if it will be repeatedly accurate. For producers to feel confident in a needle-free injection device, the accuracy and precision should be determined for the range of compounds that may be used.

The objective of this study was to validate the accuracy and precision of the Pulse Micro-Dose Injection Device (Felton International, Lenexa, KS) using several commercially available injectable products: Draxxin™ (tulathromycin, 100 mg/mL, Pfizer Animal Health, Kalamazoo, MI), Excede® (ceftiofur crystalline free acid, 100 mg/mL, Pfizer Animal Health, Kalamazoo, MI), Excenel® (ceftiofur hydrochloride, 50 mg/mL, Pfizer Animal Health, Kalamazoo, MI), and sterile water as a control (Bimeda Animal Health, Inc., Riverside, MO).

Procedure

This trial was conducted in two stages. The first stage verified the accuracy and precision of various antibiotics injected into a serum bottle through the needle-free injection device when compared to a control (sterile water). The second stage involved measuring accuracy and precision of the needle-free injection device while injecting into cadaver tissues.

Methods – Study 1

For the first stage, an empty serum bottle packed with steel wool was weighed to the nearest 0.001 g and the balance (Model GD-503-NTEP, Sartorius, Goettingen, Germany) was tared. The Micro-dose Injection device was adjusted to the desired volume setting (0.1, 0.2, 0.3, 0.4, or 0.5 mL). Product (Draxxin, Excede, Excenel, or sterile water) was injected into the serum bottle. The serum bottle was again weighed post-injection. To determine the accuracy and precision of the Micro-dose Injection Device, the volume of product injected into the serum bottle was calculated as follows: serum $\text{bottle}_{(\text{post-injection\_tared})} \div \text{specific gravity}_{(\text{Draxxin, Excede, Excenel, or sterile water})}$ = volume injected. This process was repeated 30 times for each product at each volume setting (4 products × 5 settings).

Methods – Study 2

Carcass sections were from the neck region of piglets that died naturally or were euthanized pre-weaning. Sudan Black dye (Hardy Diagnostics, Santa Maria, CA) was added to the Excenel® and Excede® and green food coloring (Adams Extract™, Gonzales, TX) was added to the Draxxin™ and sterile water before being injected into the carcass sections. Carcasses were frozen to prevent degradation. At the onset of the trial, previously frozen carcasses were stored at room temperature overnight to thaw. Each carcass section was weighed to the nearest 0.001 g and the balance was tared. The carcass section was injected with one of the four products (Draxxin, Excede, Excenel, or sterile water) at one of five volume settings (0.1, 0.2, 0.3. 0.4, and 0.5 mL) with the Micro-dose Injection Device. The carcass section was again weighed to the nearest 0.001 g post-injection. To measure product that remained on the skin surface, a cotton swab was weighed to the nearest 0.001 g and the balance was tared. Product not absorbed into the carcass was wiped up with the cotton

swab and again weighed to the nearest 0.001 g after wiping off the injection site. The amount of product injected into the carcass section was calculated as follows: ($carcass_{(post\text{-}injection\_tared)}$ – $cotton\ swab_{(post\text{-}injection\_tared)}$) ÷ $specific\ gravity_{(Draxxin,\ Excede,\ Excenel,\ or\ sterile\ water)}$) = volume of product injected. This procedure was repeated 10 times for each product at each volume setting (4 products × 5 settings).

Statistical analysis was performed using Factorial Design ANOVA in Statistix (Statistixv8.0, Analytic Software). Independent (input) variables were "trial-type" (study 1 vs. study 2), "product" (one of the four), and "dose setting" (0.1 through 0.5 mL). Dependent (outcome) variable was "injected volume" (amount in bottle or amount in carcass minus surface residue). Additionally two-way and three-way interaction terms were included in this model. All recorded weights were converted to volumes by adjusting for each product's specific gravity as previously described.

Results

Factorial Design ANOVA was used to compare the delivery error for each of the four different injectable products. Delivery error is defined as the difference between the set dose on the injection device compared to the amount injected into the bottle or carcass. Significant differences in delivery error were observed amongst products. All products except Excenel differed from sterile water (Table 1). When comparing the delivery error by the different volume settings, dose setting of 0.2, 0.3. 0.4mL differed significantly from 0.1 and 0.5mL. Dose settings of 0.1 and 0.5mL did not differ significantly (Table 1). Further, when comparing data from study 1 to data from study 2, delivery error measurements were significantly greater in study 2 than study 1 (Table 1). When examining Tukey HSD All-Pairwise Comparison, there was a linear trend of decreasing error as dose increased in study 1. Dose by product interaction showed that Excenel at 0.5mL dose was significantly different than all other dose by product interactions. No other apparent trends were observed. Using the sum of squares values generated in ANOVA, all terms and interaction terms were found to account for approximately 71% of the variation in delivery error.

Conclusions and clinical relevance

Factorial Design ANOVA revealed many differences amongst variable components and significant interaction was found between all terms. Furthermore, a large proportion of the variation was explained by the model (71%). Other influencers would be due to random effect or factors not measured.

There are several possible explanations for the differences observed. Differences between products may be due to differences in their physical properties (i.e. viscosity). Dosage settings on the equipment were pre-calibrated; therefore if the factory calibration is incorrect, delivery error differences could be explained to the degree of that error. Lastly, there may have been unknown systematic differences between the bottle and carcass trial to explain the differences found here.

Table 1: Delivery error of model of factorial ANOVA components. Different letters denote statistical differences at $P < 0.05$.

		Mean delivery error (mL)
Trial type	Study 2 (carcass)	0.0050[a]
	Study 1(bottle)	0.0018[b]
Dose setting	.3mL	0.0039[a]
	.4mL	0.0037[a]
	.2mL	0.0037[a]
	.1mL	0.0029[b]
	.5mL	0.0028[b]
Product	Excede	0.0075[a]
	Draxxin	0.0032[b]
	Excenel	0.0017[c]
	Water	0.0012[c]

Table 2: Simple cost calculations.

Product	Delivery error X cost/mL	Extra cost/mL	Dose/13# pig (mL)	Extra cost/13# pig
Excede	0.0075mL*$0.849	$0.006	0.3	$0.002
Draxxin	0.0032mL*$3.225	$0.010	0.2	$0.002
Excenel	0.0021mL*$0.611	$0.001	0.5	$0.001

Although there were statistically significant differences in delivery error between trial type, product, and volume setting, the magnitude of delivery error was very small. The overall mean delivery error was 0.0026 mL. Simple cost calculations would reveal that the differences observed between products are practically irrelevant (Table 2). Assuming the cost of Excede is $189.99/100mL bottle, Draxxin is $379.95/100mL bottle, and Excenel is $69.99/100mL bottle, the average extra cost due to delivery error would be between $0.010 and $0.001/pig treated. Even the most extreme effect observed would only have a minor impact in a 1,000 head group of pigs: 0.005 mL/pig × 1,000 pigs = 5 mL of extra product would be used in that barn. This would increase the medicine cost to this producer by $7.80 ($1.56 average cost of products/mL × 5mL of extra product) for this group of 1,000 pigs. Producers can feel confident in the relative accuracy and precision of this device.

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