

Topical Metered-Dosing Dispenser Performance Evaluation

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SIGNATURES

The reported methods and procedures contained in this report were found to describe those used and the results to constitute an accurate and complete reflection of the study raw data.



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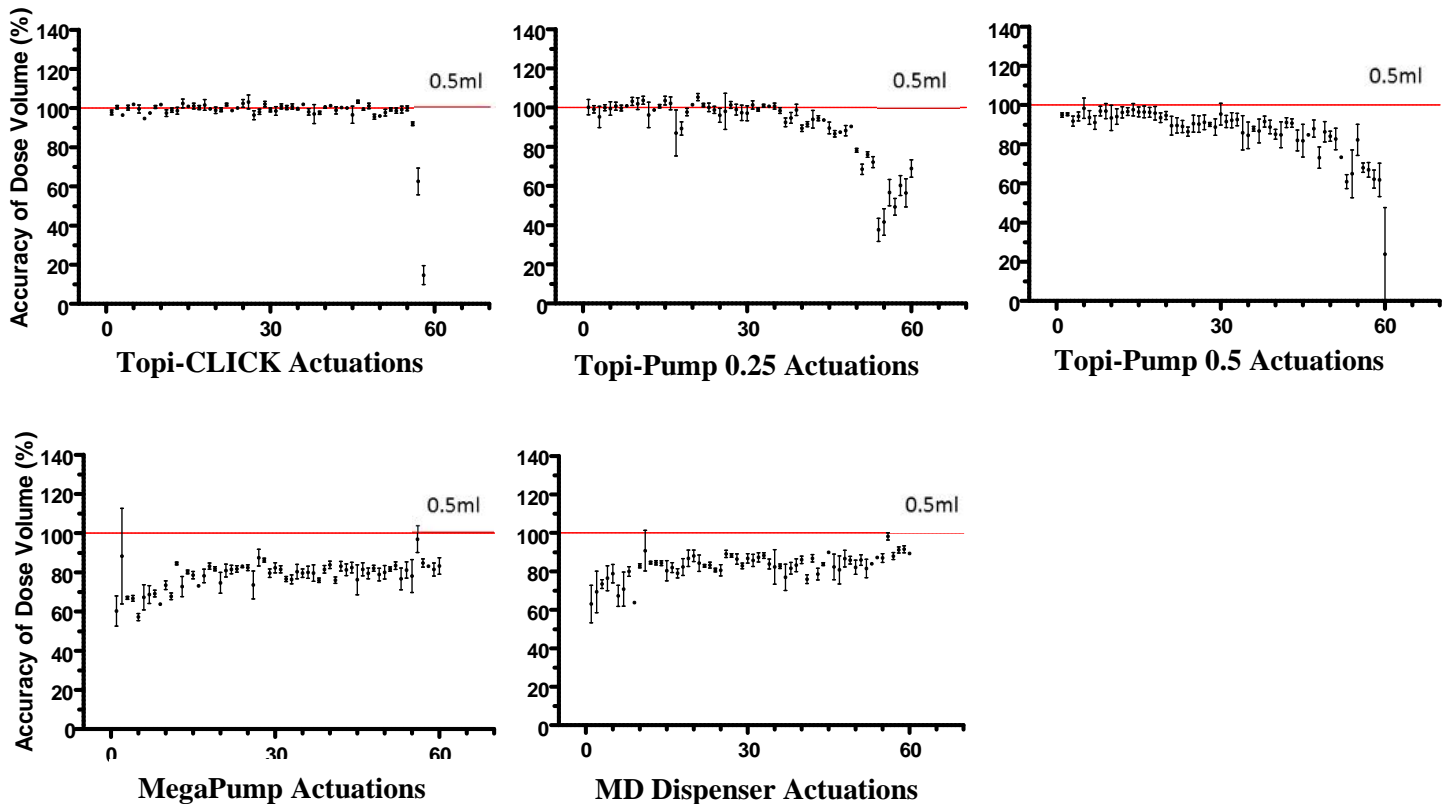
ABSTRACT

The objective of this study was to evaluate the accuracy, precision, and residual of current topical metered-dosing Dispensers (Dispensers) using three different types of topical creams for practical application. Triplicate samples of 5 different Dispensers were tested (Table A). This test was completed using three (3) types of commercial topical cream-bases of dissimilar total API Load Percentages, Transdermal Penetration Percentages and Specific Gravities. The Dispensers were evaluated according to specified criteria for dose uniformity of each actuation for a total dispensing capacity of 30 mL with a 0.5 mL per dose for 60 doses. The study shows Topi-CLICK performed with remarkable precision and consistency of dosing in comparison to the airless-pump type Dispensers (Figure A). Most notably, Topi-CLICK performance was not affected by using different types of cream-bases and was independent of the operator skills.

Table A. Five metered-dosing Dispensers evaluated in this study

Dispenser Model	Dispenser Mechanism	Dispensed Volume (mL/actuation)	Label Capacity (mL)	Number of Units (n/media)	Total Units Tested
Topi-CLICK	Dial-Click syringe	0.25	30	3	9
Topi-Pump 0.25	Airless-Pump - pouch	0.25	30	3	9
Topi-Pump 0.5	Airless-Pump - pouch	0.5	30	3	9
MegaPump	Airless-Pump - piston	0.5	30	3	9
MD Dispenser	Airless-Pump - piston	0.5	30	3	9

Figure A: Graphs of Dispensers Dosing Medium Cream



STUDY OVERVIEW

The purpose of this study was to evaluate the performance of five commercially available metered-dosing dispensers (Dispensers) in delivering the label number of doses with different types of topical cream-bases (Figure 1). Included in this study were five Dispensers represented by four marketed brands: Topi-CLICK[®], Topi-Pump[®], MegaPump[™], and MD[™] Dispenser. The major difference among these Dispensers is the mechanisms for dispensing their contents. Other design variations include the number of actuations required to dispense a 0.5 mL dose and one of the Dispensers having an applicator upon which the topical dose is dispensed.

The five Dispensers analyzed were: the Topi-CLICK (0.25 mL/actuation), Topi-Pump (0.25 mL/actuation), Topi-Pump (0.5 mL/actuation), MegaPump (0.5 mL/actuation), and MD Dispenser Pump (0.5 mL/actuation). Each Dispenser has a label capacity for 30 mL or 60 doses at 0.5 mL per dose. The Topi-CLICK (0.25 mL/actuation) and Topi-Pump (0.25 mL/actuation) require two actuations to dispense the 0.5 mL target dose, whereas the Topi-Pump (0.5 mL/actuation), MegaPump, and MD Dispenser Pump dispense the 0.5 mL dose in a single actuation. To determine the uniformity of the dispensed amounts throughout the life of each Dispenser unit, the accuracy and consistency in dispensing the target dose of 0.5 mL were assessed for a total of 60 doses, or until no further cream-base could be dispensed with actuation, using three different commercially available cream-bases for test media. These three readily available cream-bases are typical cream-bases used in compounding of topical preparations. To represent the variations in the types of cream-bases used in compounding, these three cream-bases were selected having dissimilar Total API Load Percentages, Transdermal Penetration Percentages, and Specific Gravities. Properties of the cream-bases used in this study are listed in Table 2 and can be accessed at the manufacturer's web site listed in the references¹⁻³.

Table 1. Design variations of the five tested topical metered-dose Dispensers.

Dispenser	Dispenser Mechanism	Label Quantity of Dispenses at 0.5 mL per Dose	Dispensed Volume (mL/actuation)
Topi-CLICK	Dial-click syringe with applicator	60	0.25
Topi-Pump 0.25	Airless pump with collapsible pouch	60	0.25
Topi-Pump 0.5	Airless pump with collapsible pouch	60	0.5
MegaPump	Airless pump with piston	60	0.5
MD Dispenser	Airless pump with piston	60	0.5

TESTING PROCEDURE

Preparation of the Dispensers

The entire experiment was conducted by one operator. The weights of empty Dispenser assemblies without their protective caps were recorded (Table 7). Then, each unit was completely filled with cream-base. During the filling process the Dispensers were tapped every one third (1/3) of the total unit's volume to remove air bubbles. The filled units were weighed before and after priming (Table 4). Each Dispenser was primed by actuating until approximately 30 mL of cream-base remained in the Dispenser (Table 4). The net volume for each test unit was then calculated using the specific gravity of the corresponding cream-base (Table 2 & 4). The specific gravities of the cream-bases are listed in Table 2. A total of 9 test units were prepared for each type of Dispenser, three (3) replicate test units for each of the 3 different cream-bases: thin, medium, and thick (Table 2 & 3).

Dose Measurement

Dose measurements were conducted by weighing each prepared test unit (without the protective cap) before and then, after dispensing a dose and wiping the dispensing port clean with a lint-free wipe. The test units were allowed to rest for a minimum of 2 hours between doses. This same procedure was repeated to measure 4 doses per day for a total of 60 doses or until no further cream-base could be dispensed with actuation. The final weights of the Dispensers were then obtained to determine the amount of residual cream that was unable to be dispensed. Dose measurements were converted to the volume amounts based on the specific gravity of each cream-base and were expressed in percentage of the target volume 0.5 mL/dose, as shown in the graphs of Figure 1 (page 9).

Table 2. Properties of the cream-bases¹⁻³

Cream-base Identifier	Specific Gravity (to water)	Total API Load	Transdermal Penetration
Thin	1	35%	80%
Medium	0.96	30%	70%
Thick	0.9	20%	40%

Table 3. Experiment Parameters

Dispenser	Actuations per 0.5 mL dose	Number of doses/day	Minimum Resting time (hrs.)	Total number of 0.5 mL Doses per Dispenser	Number of units tested (n/cream-base)	Total units Tested (N/Dispenser)
Topi-CLICK	2	4	2	60	3	9
Topi-Pump 0.25	2	4	2	60	3	9
Topi-Pump 0.50	1	4	2	60	3	9
MegaPump	1	4	2	60	3	9
MD Dispenser	1	4	2	60	3	9

RESULTS and DISCUSSIONS

The net weight of each Dispenser's cream-base amount was converted to the volume amount (mL) for each group of Dispensers (Table 4). This data represents the amount of cream-base in the Dispensers after priming to approximately 30 mL for all test units with no overfill volume. Dose uniformity (as specified below) was assessed based on the dispensed amount for the total 60 doses indicated in Table 3.

The Dispenser's performance with each cream-base is profiled in the graphs shown in Figure 1. It should be noted that no Dispenser completed full 60 doses during the experiment. Actual and average volumes for the dispensed amounts at actuations "1 of 60", "30 of 60" and "50 of 60" are shown in Table 5. The number of doses found within specified limits for uniformity are presented in Table 6 for each test group, and calculated as percentage of the total 60 doses.

Individual dose uniformity is defined as an amount equivalent to 75-125% of the target dose, and the average amount for 3 replicate test units is within 85-115% of the target dose (as defined by FDA Draft Guidance for Industry shown in references⁴). Included in Table 7 is the amount of residual cream in the Dispensers after no amount of cream-base could be further dispensed with actuation.

Topi-CLICK

The data shows that all Topi-CLICK test units accurately and precisely dispensed the cream-base within 75-125% of the target dose volume until 88.3-98.3% of the total 30 mL had been dispensed (Table 6, Figure 1). The performance of Topi-CLICK was not affected by the different types of cream-base. The entire range of the 88.3-98.3% of doses dispensed by Topi-CLICK units met the acceptance criteria for uniformity of doses (Table 5 & 6).

When the Topi-CLICKs completed dispensing, the average amounts of residual cream were 2.3-2.5 mL (Table 7).

Topi-Pump 0.25

The data shows that overdosing initially occurred with the Topi-Pump 0.25 when dispensing the "thin" cream-base. Multiple doses exceeded the upper limit of 115% of the target dose volume (Figure 1). The average volume for the dispensed amounts at actuation "1 of 60" was 118.1% of the target (Table 5). Additionally, underdosing developed after approximately 44 doses. The average volume for the dispensed amounts at actuation "50 of 60" was 53.5% of the target (Table 5). Due to the initial overdosing the Topi-Pump 0.25 prematurely dispensed below the lower limit of 85% (Figure 1). On average, only 45% of the total doses dispensed were within range for dose uniformity when using the "thin" cream (Table 6).

The “thick” cream-base had similar effect on the performance of Topi-Pump 0.25, albeit to a lesser degree. Underdosing developed after approximately 47 doses (Figure 1). The range for average dispensing was 14.6-116.4% of the target 0.5 mL dose (Figure 1), and 76.7% of the total 60 doses were within range for dose uniformity (Table 6). The Topi-Pump 0.25 improved with the “medium” cream-base where at least 80.0% of doses dispensed were within the limits of 85-115%, and underdosing occurred after 50 doses or after approximately 81.7% of total doses had been dispensed (Table 6, Figure 1).

When the Topi-Pump 0.25 completed dispensing, the average amounts of residual cream were 2.0-3.6 mL (Table 7).

Topi-Pump 0.5

Topi-Pump 0.5 operates the same as the Topi-Pump 0.25 with the exception that single actuation dispensed the target dose volume of 0.5 mL. Therefore, it was not unexpected to observe a similar performance profile between the two pumps. Although doses larger than 115% of target did not occur with Topi-Pump 0.5, the data shows that the patterns of dispenses were high for the first 30 doses with the “thin” cream-base (Figure 1). The average initial dose was 112.3% of target, and more than 100% of target for most of the first 30 doses (Table 5). Underdosing developed after 42 doses or after approximately 70% of total doses had been dispensed (Figure 1). Similarly, the range of average dose was 97.7-109.9% of target in the first 50% of doses with the “thick” cream-base, and underdosing occurred after approximately 75% of the total doses had been dispensed (Figure 1). The percentages of doses within range for dose uniformity were 71.7% and 75.0% for the “thin” and “thick” cream-base respectively (Table 6). In contrast, the “medium” cream was dispensed at lower doses with higher variability (dose range 23.8-98.3% of target), and 68.3% of doses were deemed within limits for dose uniformity (Figure 1, Table 6).

When the Topi-Pump 0.5 completed dispensing, the average amounts of residual cream were 3.8-4.5 mL (Table 7).

MegaPump

The test results show that the MegaPump was unsuitable for use with the “medium” cream-base, as a majority of doses were low and highly variable (Figure 1). Table 6 shows only 5.0% of total doses were within range for dose uniformity. Figure 1 shows average dispenses varied from 57.2% to 96.9% of the target dose. In general, the MegaPump exhibited lower volume dispenses initially (Figure 1, Table 5). On average, approximately 78.3-83.3% of the total doses were dispensed successfully using “thin” or “thick” cream-bases (Table 6). The range of averaged dispensed amounts were 36.6-104.3% and 67.2-

102.7% of target dose volume for “thin” and “thick” cream-bases respectively (Figure 1). However, more instances of underdosing were experienced using the “thick” than “thin” cream-bases.

When the MegaPump completed dispensing, the average amounts of residual cream were 1.4-1.6 mL (Table 7).

MD Dispenser

The data shows the MD Dispenser also was unfavorable for dispensing the “medium” cream-base, with only 38.3% of the total doses within range for dose uniformity (Table 6). The average amounts varied between 63.0-90.8% of the target dose and many dispenses failed the specified criteria for dose uniformity (Figure 1). There was minimal difference in the MD Dispenser performance with the “thin” and “thick” cream-bases, respectively 81.7% and 83.3% of the total doses dispensed within range for dose uniformity (Table 6). An overdosing trend is shown with the “thin” and “thick” cream-bases (Figure 1).

When the MD Dispenser completed dispensing, the average amounts of residual cream were 1.9-2.1 mL (Table 7).

CONCLUSION

Overall, the study shows Topi-CLICK performed with remarkable precision and accuracy compared to the other Dispensers. Most remarkably, Topi-CLICK performance did not vary from one cream-base type to the next. Therefore, Topi-CLICK was not affected by the three different types of cream-bases used in this study, and seemed to be easier to use.

Most notable was all four of the airless pump type Dispensers showed more variation and sensitivity to the different properties in the three cream-bases.

Additionally noted, the airless pumps with collapsible pouch (both Topi-Pumps) demonstrated the most premature decline in overall dispensing. Also of note, both Topi-Pump Dispensers had a characteristic of initial overdosing followed by underdosing with “thin” and “thick” cream-bases, and not with the “medium” cream-base.

The airless pumps with piston (MegaPumps and MD Dispensers) underdosed failing to dispense the label target volume within acceptable range with the “medium” cream-base.

Regarding the residual cream-base amounts of all Dispensers, the MegaPumps and MD Dispensers had the least amount of residual cream, and the Topi-Pumps had the most residual cream after completion.

Figure 1. Performance Graphs of Dispensers. Average (n=3) dispensed amount in % relative to the target 0.5 mL dose volume for the total label number of doses. Horizontal line indicates 0.5 mL (100%).

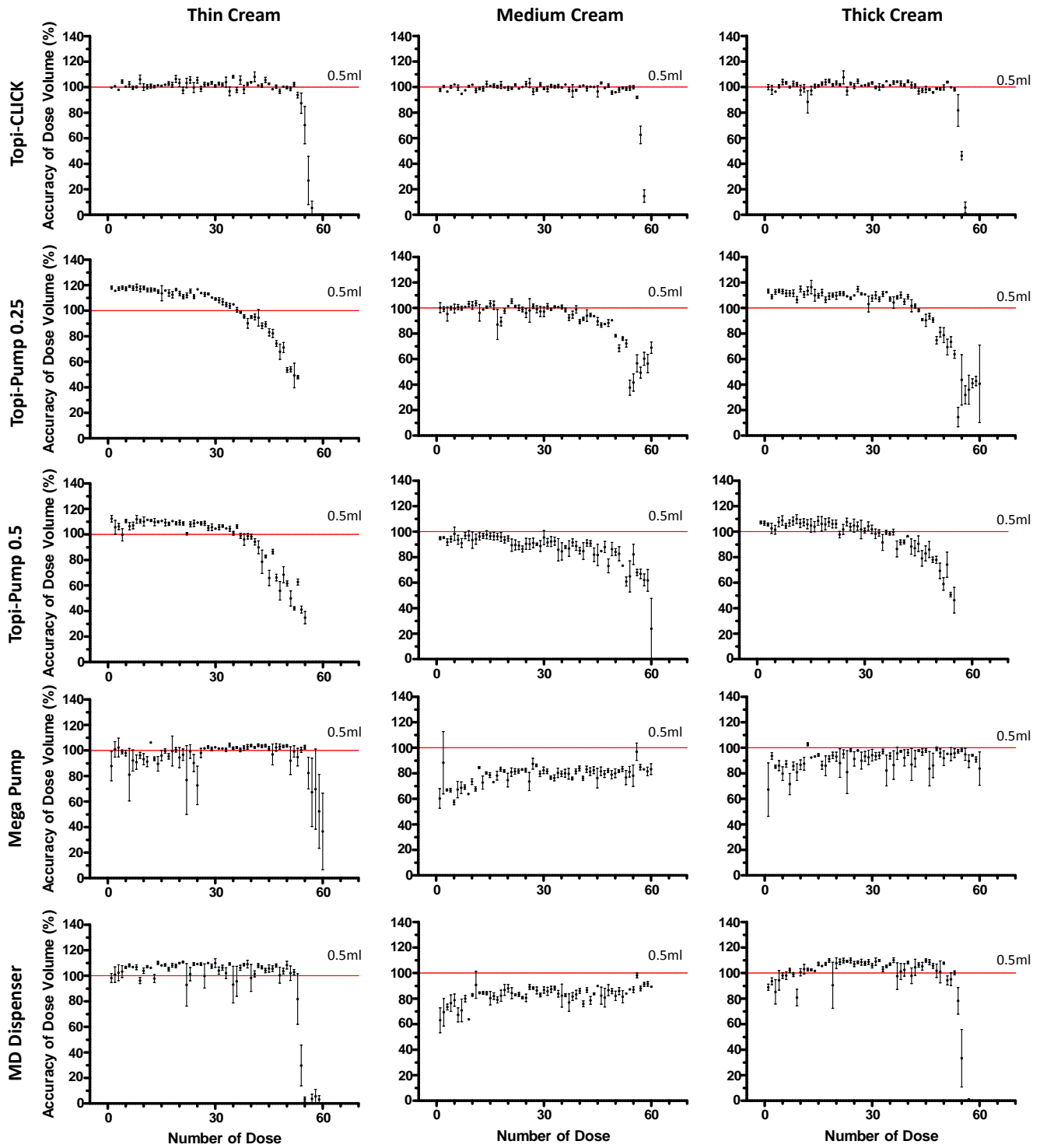


Table 4. Beginning volume (mL) of cream-base after priming in Dispenser. Volume (mL) calculated based on cream-base specific gravity (Table 2).

Topi-CLICK	Filled Dispenser Weight (g)			Dispenser Weight After Priming (g)			Beginning Cream-base Weight (g)			Beginning Cream-base Volume (mL)		
	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	72.59	71.22	70.79	67.22	65.85	63.67	30.82	29.48	27.47	30.82	30.71	30.52
2	71.94	71.12	70.34	66.70	66.12	63.52	30.32	29.76	26.99	30.32	31.00	29.98
3	71.95	71.20	69.75	66.39	66.09	63.36	29.98	29.70	27.11	29.98	30.94	30.13
Topi-Pump 0.25	Filled Dispenser Weight (g)			Dispenser Weight After Priming (g)			Beginning Cream-base Weight (g)			Beginning Cream-base Volume (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	58.11	53.66	52.17	53.45	51.83	50.12	30.97	29.34	27.96	30.97	30.56	31.07
2	57.94	54.35	52.99	53.08	52.10	50.12	30.47	29.85	27.62	30.47	31.09	30.69
3	57.79	54.08	53.18	53.31	52.28	50.14	30.81	29.72	27.65	30.81	30.95	30.72
Topi-Pump 0.5	Filled Dispenser Weight (g)			Dispenser Weight After Priming (g)			Beginning Cream-base Weight (g)			Beginning Cream-base Volume (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	65.80	64.94	64.52	62.72	62.08	60.01	30.13	29.46	27.59	30.13	30.69	30.65
2	66.48	65.98	64.47	62.89	62.09	60.01	30.34	29.40	27.47	30.34	30.62	30.52
3	66.26	65.29	64.78	63.99	62.07	60.01	31.35	29.49	27.50	31.35	30.72	30.56
MegaPump	Filled Dispenser Weight (g)			Dispenser Weight After Priming (g)			Beginning Cream-base Weight (g)			Beginning Cream-base Volume (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	61.62	55.21	53.27	53.57	53.29	50.67	30.23	29.96	27.43	30.23	31.21	30.48
2	54.88	55.32	53.27	53.77	53.11	50.41	30.47	29.69	27.13	30.47	30.92	30.15
3	58.11	56.04	52.91	53.73	53.05	50.59	30.46	29.74	27.16	30.46	30.98	30.18
MD Dispenser	Filled Dispenser Weight (g)			Dispenser Weight After Priming (g)			Beginning Cream-base Weight (g)			Beginning Cream-base Volume (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	84.36	81.38	79.54	77.53	76.96	74.60	30.19	29.50	27.10	30.19	30.73	30.11
2	82.77	78.84	79.66	77.87	76.97	74.56	30.49	29.49	27.18	30.49	30.72	30.20
3	81.97	79.82	78.98	77.63	76.08	74.55	30.14	28.72	27.08	30.14	29.91	30.09

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Table 5. Actual and average volumes for the dispensed amounts at actuations “1 of 60”, “30 of 60” and “50 of 60”. Average results are average of n = 3 Dispensers. Dispensed amounts determined as percentage of the target dose volume 0.5 mL.

Topi-CLICK	Volume of Actuation "1 of 60" (mL)			Volume of Actuation "30 of 60" (mL)			Volume of Actuation "50 of 60" (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	0.497	0.481	0.496	0.498	0.485	0.517	0.495	0.483	0.506
2	0.502	0.501	0.520	0.513	0.500	0.523	0.508	0.480	0.511
3	0.496	0.484	0.483	0.503	0.500	0.509	0.493	0.476	0.479
Average	0.498	0.489	0.500	0.505	0.495	0.516	0.499	0.480	0.499
% of Target	99.7%	97.8%	99.9%	100.9%	99.0%	103.3%	99.7%	96.0%	99.7%
Topi-Pump 0.25mL	Volume of Actuation "1 of 60" (mL)			Volume of Actuation "30 of 60" (mL)			Volume of Actuation "50 of 60" (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	0.579	0.525	0.580	0.538	0.501	0.562	0.286	0.389	0.429
2	0.601	0.516	0.563	0.553	0.507	0.522	0.257	0.400	0.416
3	0.592	0.463	0.554	0.546	0.448	0.530	0.260	0.383	0.336
Average	0.591	0.501	0.566	0.546	0.485	0.538	0.268	0.391	0.393
% of Target	118.1%	100.2%	113.2%	109.1%	97.1%	107.6%	53.5%	78.1%	78.7%
Topi-Pump 0.5mL	Volume of Actuation "1 of 60" (mL)			Volume of Actuation "30 of 60" (mL)			Volume of Actuation "50 of 60" (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	0.581	0.464	0.528	0.523	0.529	0.500	0.316	0.425	0.413
2	0.565	0.482	0.546	0.526	0.467	0.522	0.288	0.396	0.366
3	0.538	0.477	0.533	0.519	0.434	0.490	0.319	0.440	0.389
Average	0.561	0.474	0.536	0.523	0.477	0.504	0.308	0.420	0.389
% of Target	112.3%	94.9%	107.1%	104.5%	95.3%	100.8%	61.5%	84.0%	77.9%
MegaPump	Volume of Actuation "1 of 60" (mL)			Volume of Actuation "30 of 60" (mL)			Volume of Actuation "50 of 60" (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	0.503	0.316	0.420	0.509	0.411	0.496	0.512	0.366	0.497
2	0.489	0.229	0.128	0.517	0.433	0.426	0.528	0.415	0.402
3	0.324	0.359	0.460	0.511	0.390	0.492	0.514	0.420	0.479
Average	0.439	0.301	0.336	0.512	0.411	0.471	0.518	0.400	0.459
% of Target	87.7%	60.3%	67.2%	102.5%	82.3%	94.2%	103.6%	80.0%	91.9%
MD Dispenser	Volume of Actuation "1 of 60" (mL)			Volume of Actuation "30 of 60" (mL)			Volume of Actuation "50 of 60" (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	0.504	0.370	0.423	0.516	0.433	0.542	0.516	0.389	0.546
2	0.513	0.357	0.446	0.563	0.455	0.512	0.569	0.396	0.537
3	0.456	0.218	0.464	0.570	0.413	0.533	0.540	0.447	0.533
Average	0.491	0.315	0.444	0.550	0.434	0.529	0.542	0.410	0.539
% of Target	98.2%	63.0%	88.9%	109.9%	86.7%	105.9%	108.3%	82.1%	107.7%

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Table 6. Percentage of 60 dispenses within limits for dose uniformity after primed to approximately 30 mL (Table 2). Table values are based on average of n = 3 test units.

Dispenser	Doses within Uniformity Limits*		
	Thin	Medium	Thick
Topi-CLICK	88.30%	96.70%	98.30%
Topi-Pump 0.25	45.00%	80.00%	76.70%
Topi-Pump 0.5	71.70%	68.30%	75.00%
MegaPump	83.30%	5.00%	78.30%
MD Dispenser	81.70%	38.30%	83.3.0%

**Criteria for dose uniformity: Individual actuation within 75-125% of target dose and average dispensing within 85-115% of target dose for n = 3 test units.*

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Topical Metered-Dosing Dispenser Performance Evaluation

Table 7: Data of remaining residual cream in Dispensers. (Amount of cream-base left in Dispenser when no amount of cream-base can be further dispensed with actuation). Volume (mL) calculated based on cream-base specific gravity (Table 2).

Topi-CLICK	Weight of Empty Dispenser (g)			Final Weight of Dispenser at completion (g)			Remaining Cream-Base (g)			Remaining Cream-Base (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	36.39	36.38	36.52	38.73	38.75	38.82	2.34	2.38	2.3	2.34	2.48	2.55
2	36.38	36.37	36.49	38.63	38.72	38.68	2.24	2.35	2.18	2.24	2.45	2.42
3	36.41	36.39	36.41	38.75	38.78	38.65	2.34	2.39	2.24	2.34	2.49	2.49
Average	36.39	36.38	36.47	38.70	38.75	38.72	2.31	2.37	2.24	2.31	2.47	2.49
Topi-Pump 0.25mL	Weight of Empty Dispenser (g)			Final Weight of Dispenser at completion (g)			Remaining Cream-Base (g)			Remaining Cream-Base (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	22.48	22.49	22.16	26.29	25.18	23.99	3.81	2.69	1.83	3.81	2.81	2.03
2	22.61	22.26	22.5	26.14	25.01	24.32	3.53	2.75	1.82	3.53	2.86	2.02
3	22.5	22.56	22.49	25.88	25.47	24.17	3.39	2.9	1.68	3.39	3.02	1.87
Average	22.53	22.44	22.38	26.10	25.22	24.16	3.58	2.78	1.78	3.57	2.90	1.97
Topi-Pump 0.5mL	Weight of Empty Dispenser (g)			Final Weight of Dispenser at completion (g)			Remaining Cream-Base (g)			Remaining Cream-Base (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	32.59	32.62	32.43	36.52	36.67	36.13	3.94	4.05	3.7	3.94	4.22	4.12
2	32.55	32.69	32.54	36.23	37.45	35.51	3.68	4.76	2.97	3.68	4.96	3.30
3	32.65	32.58	32.51	36.48	36.64	36.53	3.83	4.06	4.02	3.83	4.23	4.47
Average	32.60	32.63	32.49	36.41	36.92	36.06	3.82	4.29	3.56	3.82	4.47	3.96
MegaPump	Weight of Empty Dispenser (g)			Final Weight of Dispenser at completion (g)			Remaining Cream-Base (g)			Remaining Cream-Base (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	23.34	23.33	23.24	24.85	24.78	24.59	1.51	1.46	1.36	1.51	1.52	1.51
2	23.3	23.43	23.28	24.86	25.02	24.49	1.56	1.59	1.2	1.56	1.66	1.34
3	23.27	23.3	23.43	24.87	24.9	24.75	1.61	1.6	1.33	1.61	1.66	1.47
Average	23.30	23.35	23.32	24.86	24.90	24.61	1.56	1.55	1.30	1.56	1.61	1.44
MD Dispenser	Weight of Empty Dispenser (g)			Final Weight of Dispenser at completion (g)			Remaining Cream-Base (g)			Remaining Cream-Base (mL)		
Replicates	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick	Thin	Medium	Thick
1	47.34	47.46	47.49	49.08	49.41	49.27	1.74	1.94	1.78	1.74	2.02	1.97
2	47.38	47.48	47.37	49.4	49.51	48.99	2.02	2.03	1.61	2.02	2.12	1.79
3	47.49	47.37	47.47	49.31	49.39	49.15	1.82	2.02	1.68	1.82	2.10	1.87
Average	47.40	47.44	47.44	49.26	49.44	49.14	1.86	2.00	1.69	1.86	2.08	1.88

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 - a. Since no direct guidance could be found for metered-dose topical dispensers these draft guidelines have been applied for analytical purposes for this study.