

Characterization of Nicotine Pharmacokinetic Profiles and Subjective Effect Measures for e-Vapor Products Relative to Cigarette and Nicotine Gum

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Background

- The FDA's Draft PMTA Guidance for Electronic Nicotine Delivery Systems¹ suggests that applicants include results from studies addressing abuse liability of new e-vapor products.
- To address the regulatory guidance for new tobacco product applications, these studies assessed the rate and extent of nicotine exposure and subjective measures of six MarkTen[®] e-vapor products.

¹ Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems Draft Guidance. U.S. Food and Drug Administration, Center for Tobacco Products, May 2016



Objectives

- To compare plasma nicotine pharmacokinetic (PK) parameters (C_{\max}) and subjective effects (E_{\max}) between each of Nu Mark's six MarkTen[®] e-vapor products and subjects' usual-brand cigarettes and Nicorette[®] nicotine polacrilex gum (nicotine gum) under *controlled* and *uncontrolled* use conditions
- To characterize product use behavior of the six MarkTen[®] e-vapor products, subjects' usual-brand cigarettes, and the nicotine gum under *ad libitum* use conditions

C_{\max} = maximum concentration; E_{\max} = maximum VAS score or reduction in response to the questionnaire



Study Product

	Product Flavor	Nicotine (% by weight)	Nicotine ^a (mg/puff)
Study ①	Winter Mint	3.5	0.19
	Menthol	3.5	0.21
	Menthol Bold	4.0	0.23
Study ②	Fusion	2.5	0.13
	Classic	3.5	0.19
	Classic Bold	4.0	0.20
① & ②	Cigarette ^b	Varies	
	Nicorette® Gum	4.0 mg	

^a Based on 5s puff duration, 50mL puff volume and 30s inter-puff-interval

^b Subjects' usual brand cigarettes

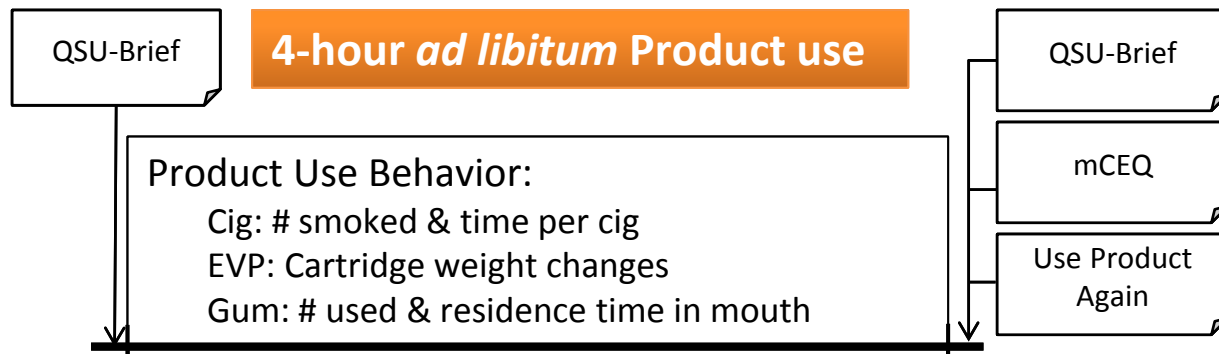
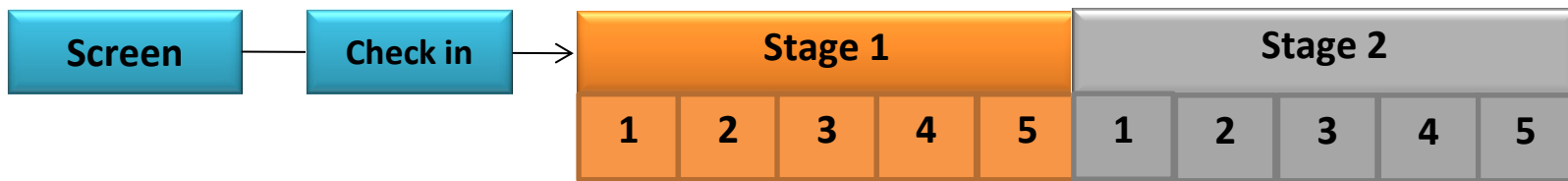


Nu Mark's MarkTen® e-vapor



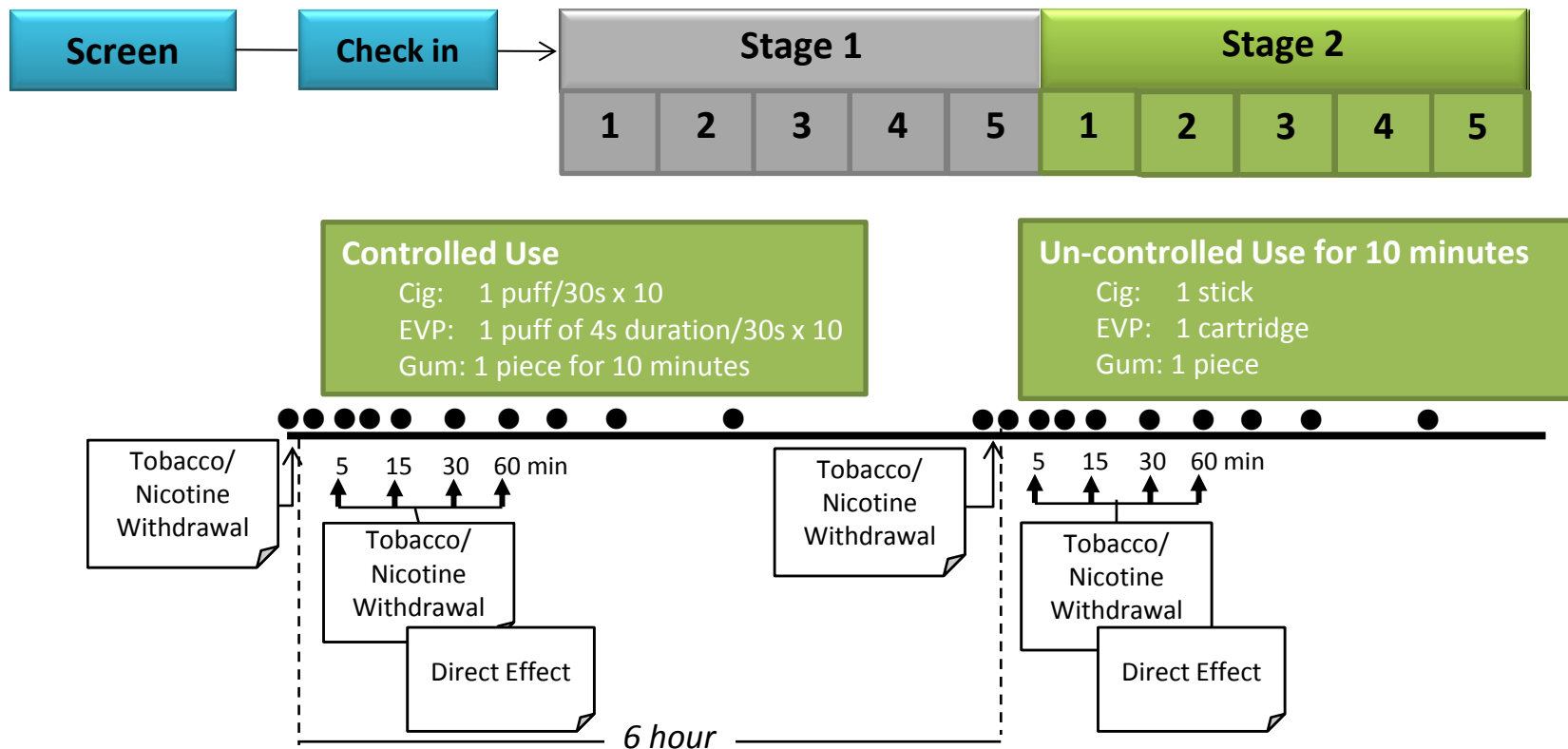
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Study Design: 5-Way Cross Over



QSU: Questionnaire of Smoking Urges; mCEQ: Modified Cigarette Evaluation Questionnaire; EVP: e-Vapor product

Study Design: 5-Way Cross Over



● blood draw at 5 minutes prior to and at 2, 5, 10, 12, 15, 20, 30, 60, 120 and 180 minutes following the start of the product use



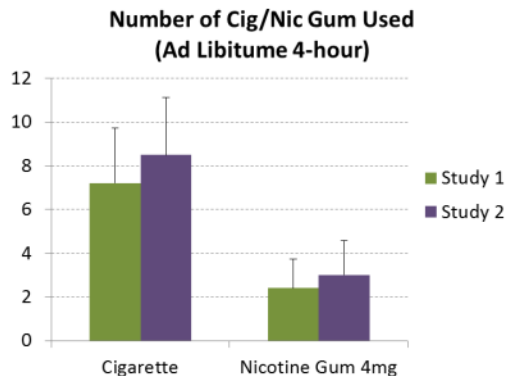
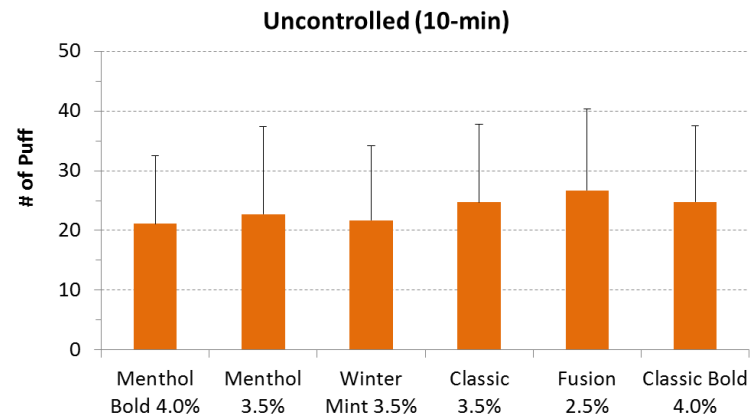
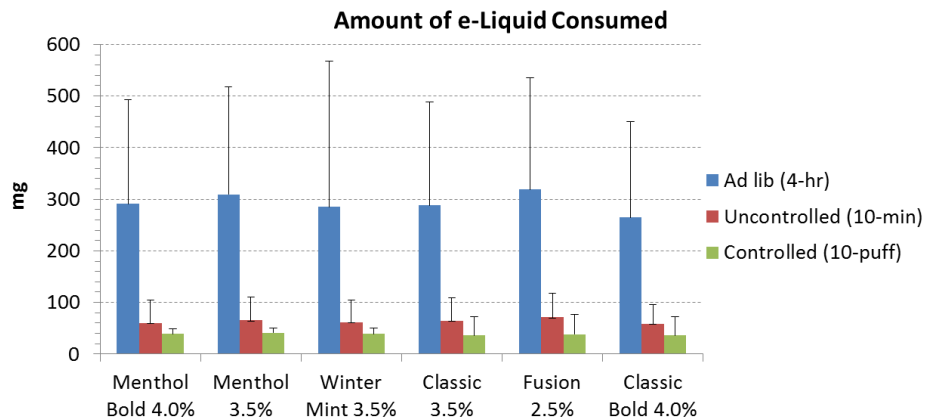
Demographics

	Study 1	Study 2
Randomized (completed)	78 (69)	83 (67)
Age (year)	35.1 ± 10.6	39.8 ± 11.0
Male	46 (59%)	48 (58%)
Female	32 (41%)	35 (42%)
Weight (kg)	76.3 ± 14.5	80.4 ± 12.5
BMI (kg/m ²)	26.2 ± 4.2	26.7 ± 3.7
CPD	11.4 ± 4.6	15.5 ± 5.1
Years Smoked	17.4 ± 10.6	22.4 ± 11.7

BMI: body mass index; CPD: cigarette per day



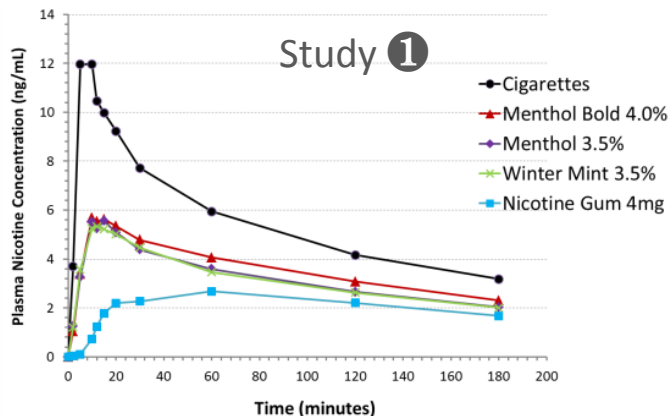
Product Use Behavior



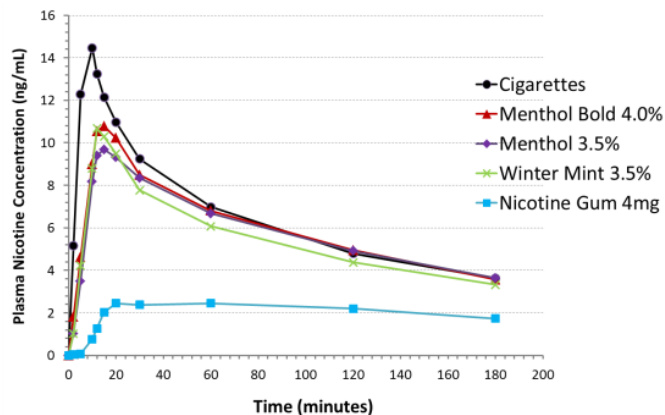
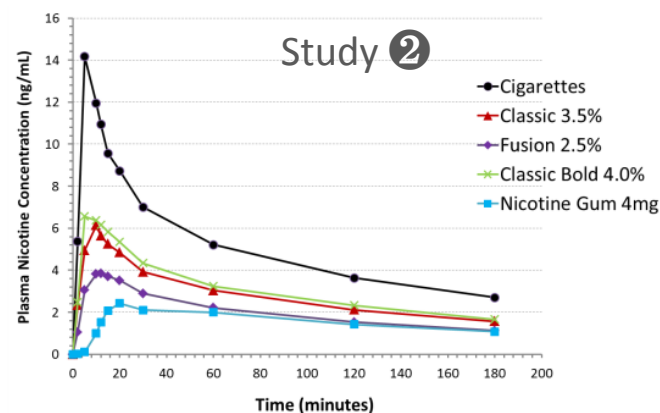
Data shown as mean \pm SD



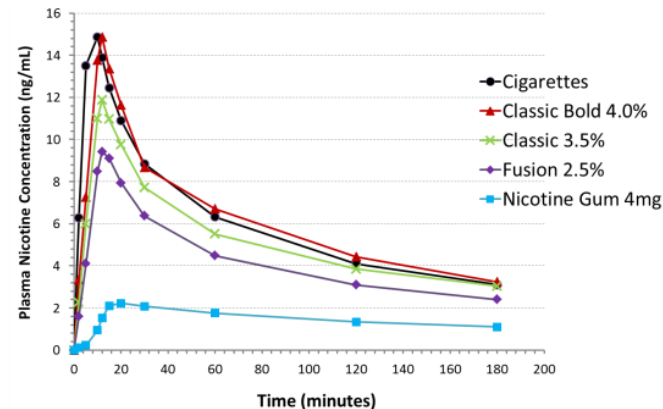
How Close are the Plasma Nicotine Levels Compared to Cigarettes?



Controlled



Uncontrolled



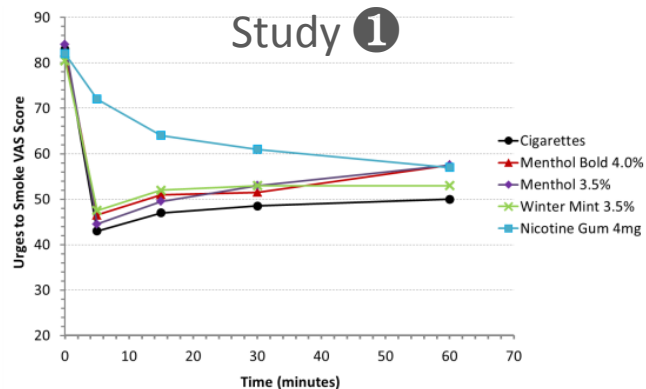
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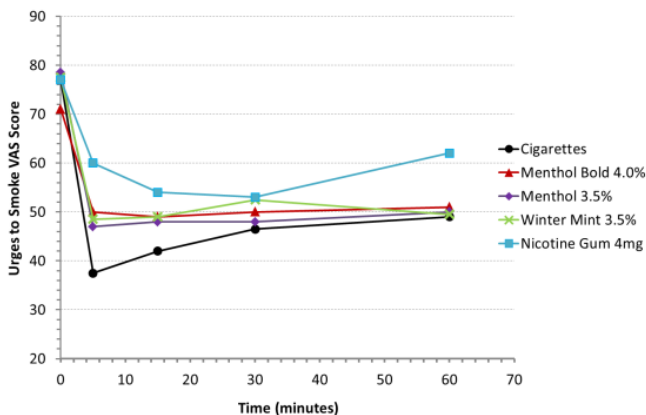
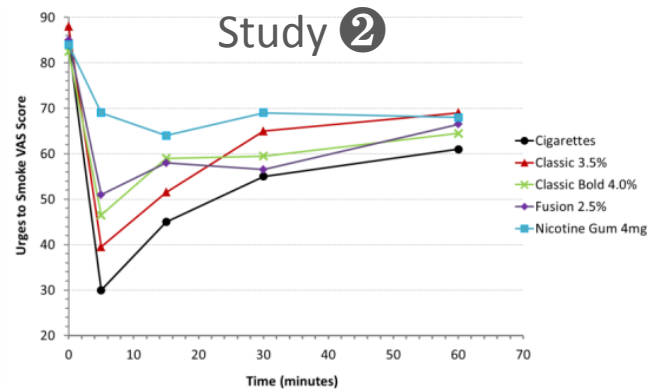
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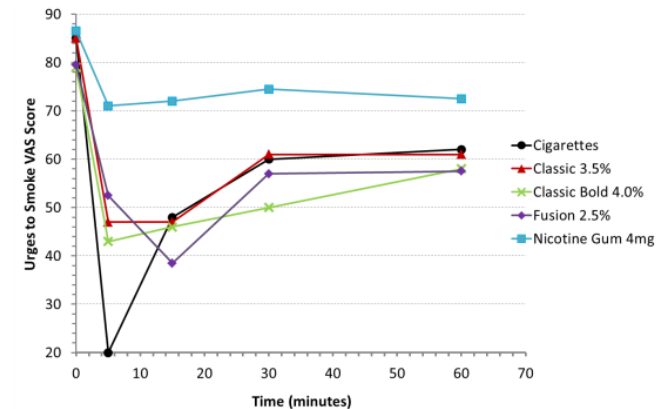
Reductions in “Urges to Smoke”



Controlled



Uncontrolled

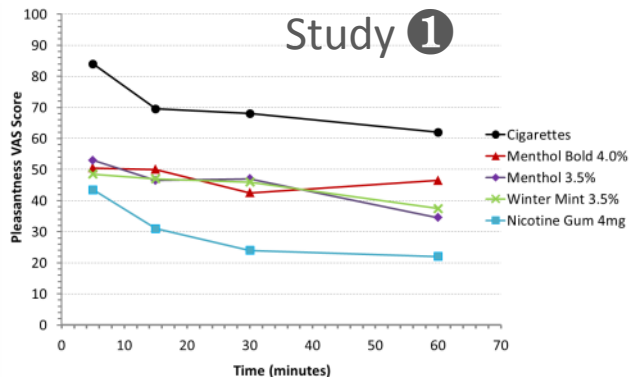


Data shown as median

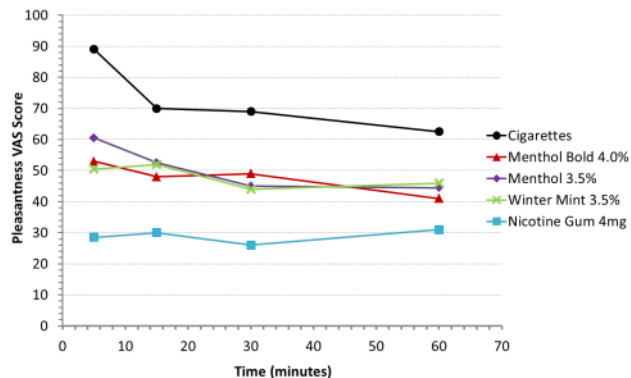
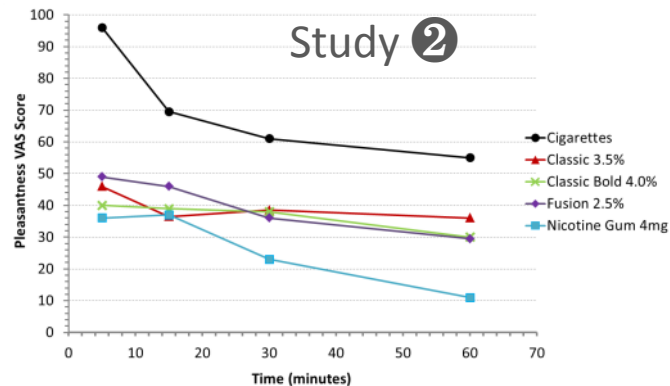


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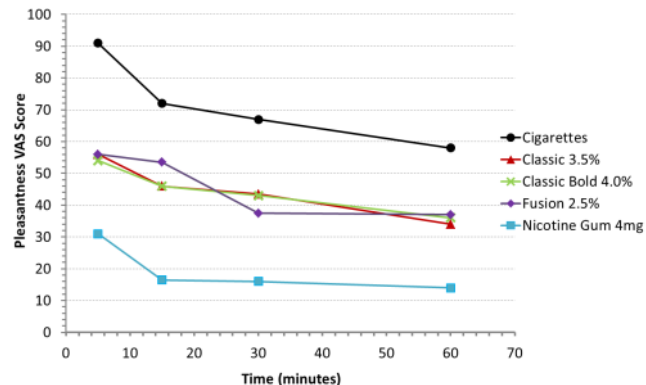
Ratings on Product “Pleasantness”



Controlled



Uncontrolled



Data shown as median



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Summary

- Use of the six MarkTen® e-vapor products under controlled use conditions are associated with statistically significant:
 - Lower peak nicotine exposures compared with subjects' usual-brand cigarettes;
 - Lower peak ratings of “pleasantness”; Lower reductions in “urges to smoke” for Winter Mint, Classic and Fusion, but not significantly different for Menthol Bold, Menthol and Classic Bold compared with subjects' usual-brand cigarettes
 - Higher nicotine exposure, greater reductions in “urge to smoke” (except Fusion) and higher “pleasantness” ratings (except Classic Bold) compared with nicotine gum.
- During the 4-hour ad libitum use period, subjects
 - Consumed approximately 300 mg of e-liquid (contained from approximately 8 mg of nicotine for Fusion [2.5%] to 12 mg of nicotine for Classic & Menthol Bold [4.0%]);
 - Smoked 7-9 cigarettes and
 - Used 2-3 nicotine gum.
- During the 10-minutes uncontrolled use, subjects
 - Took twice as many puffs from e-vapor products as they did during the controlled use condition and
 - Consumed 1.5 – 2 folds of e-liquid as they did during the controlled use condition.



Conclusion

These findings indicate that the rate and extent of nicotine exposures and subjective measures response scores from the MarkTen[®] e-vapor products are greater than nicotine replacement therapy gum but are not greater than conventional cigarettes.





Thank you!

