

Characterization of E-Vapor Product Aerosols in Two Different Exposure Regimens for a Nose-Only Rodent Inhalation System

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ABSTRACT

Inhalation studies require reliable exposure generation and characterization regardless of the type of product being tested. In this study, an established rodent nose-only inhalation exposure setup was adapted to generate aerosols from an example e-vapor product (MarkTen®) and conventional (3R4F) cigarettes using a rotary cigarette smoking machine (CSM). For the e-vapor product, aerosols were generated in two ways. The first was using the CORESTA CRM81 puffing regimen (30-sec puff interval, 3-sec puff duration, and a puff volume of 55 mL) for 180 puffs/cartridge. The second was using a modified regimen with a longer puff duration (CRM81, except for 5-sec puff duration) and a puff count of 120 to 130 puff/cartridge. The 3R4F cigarette smoke aerosols were generated using the Health Canada Intense puffing regimen (30-sec puff interval, 55ml puff volume with 2-sec puff duration). The e-vapor product CSM delivered aerosols to up to three nose-only animal exposure carousels at the target concentration of 1300 to 1400 ug/L total particulate matter (TPM) for 4 hours. The TPM, particle size distribution and selected analytes (nicotine, carbon monoxide, propylene glycol, glycerol and carbonyls) were measured at nose ports. Using the modified (5-sec) puffing regimen, the e-vapor TPM concentration met the target concentration within 6% for each exposure carousel with or without active feedback control. The MMAD was initially slightly higher for the modified regimen compared to the CRM81 regimen, however following modifications to the exposure generation system the particle size was comparable (~1.1 µm) for both e-vapor exposure regimens. Ratios of e-vapor aerosol constituents (nicotine, PG, and glycerol) were similar and did not change from the CSM to nose ports. For the 3R4F CSM connected to two exposure carousels, TPM was within 1% of target (550 ug/L), the MMAD was at ~0.7 µm and the CO/TPM ratio was ~1.2. This work provides the basis to establish repeated rodent nose-only inhalation exposure regimens.

EXPERIMENTAL DESIGN

Aerosol delivery from one smoke machine to multiple exposure carousels

- Changed from siphoning portion of aerosol from mixing bulb to using metering pumps delivering a portion of the aerosol from the mixing bulb to individual exposure carousels
- Measured gravimetric and constituent (Nicotine, Propylene Glycol, Glycerol) concentrations at output of smoke machine and at nose-port for both e-vapor product and 3R4F cigarette
- Assessed CO/TPM ratio of 3R4F cigarette at nose-port
- Assessed changes in constituent ratios at nose-port as compared to original configuration

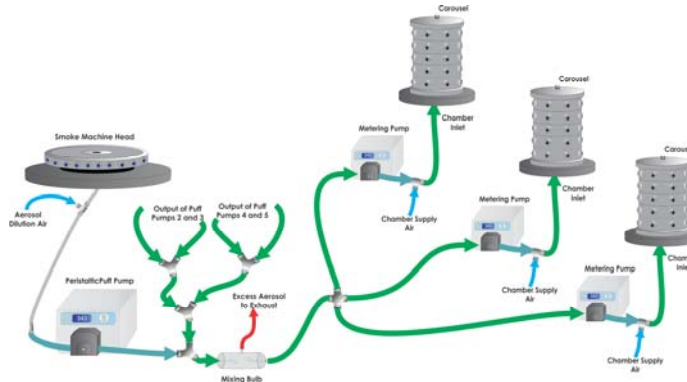
Changing puff duration from 3 seconds to 5 seconds for e-vapor product

- Modified smoke machine to add additional puff ports, moved aerosol dilution air closer to the puff ports
- Measured gravimetric and constituent concentrations at the output of the smoke machine and at the nose-port
- Measured mg/puff output based on cartridge weight loss
- Measured particle size at the output of the smoke machine and at the nose-port

Number of puffs per cartridge of e-vapor product

- Measured gravimetric concentration at the nose-port for one cartridge until no response was detected by Real time Aerosol Monitor (RAM)
- Compared nose-port data to analytical smoke machine data (provided by Sponsor)

E-Vapor Product Exposure System Schematic – Final Configuration



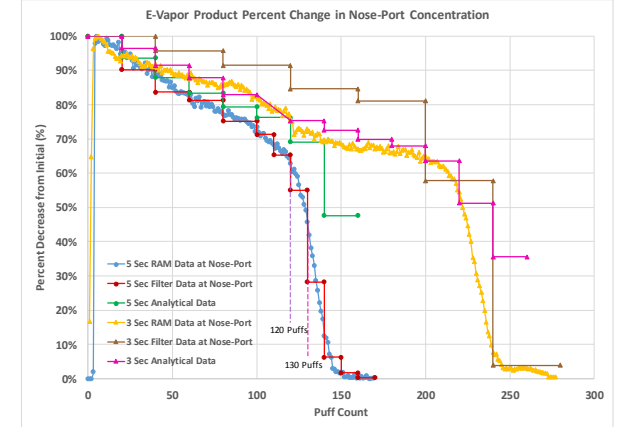
RESULTS AND DISCUSSION

E-Vapor Product							
Puff Duration / Regimen	Configuration	Sample Details	Target Gravimetric Concentration (µg TPM/L)	Gravimetric Measured Concentration (µg TPM/L)	Nic/TPM	Ratio Nose-Port Nic / CSM Nic	CO/TPM
3 Sec CRM81 180 puffs/cartridge	1 CSM to 1 Carousel	Carousel 1	1400	1412	3.3%		
		Carousel 2		1438	3.1%	89%	
		Carousel 3		1480	3.2%	90%	
		Carousel 1		1395	3.1%	87%	
5 Sec Intense 55 mL/30 sec/5 sec 120 puffs/cartridge	1 CSM to 3 Carousels	Carousel 1	1450	3.2%	91%		
		Carousel 2	1450	3.2%	91%		
		Carousel 3	1427	3.1%	89%		
		Carousel 1	1427	3.1%	89%		
3R4F Cigarette							
Puff Duration / Regimen	Configuration	Sample Details	Target Gravimetric Concentration (µg TPM/L)	Gravimetric Measured Concentration (µg TPM/L)	Nic/TPM	Ratio Nose-Port Nic / CSM Nic	CO/TPM
2 Sec Modified HCl 8 puffs/cigarette	1 CSM to 2 Carousels	Carousel 1	550	549	7.4%	109%	1.22
		Carousel 2		548	7.3%	107%	1.19
		Carousel 1		555	7.5%	111%	1.16

1. Estimated CSM usage rate on a per carousel basis considering each configuration.

- For the e-vapor product, gravimetric and constituent concentrations at the nose-port were consistent when delivering to one, two, or three exposure carousels. Constituents other than nicotine were measured and consistent among the configurations thus are not presented.
- For 3R4F, gravimetric and nicotine concentrations at the nose-port were consistent when delivering to one or two exposure carousels. CO/TPM ratio was slightly lower when delivering to two exposure carousels.

E-Vapor Product Output and Particle Size Distribution				
Puff Duration	mg/Puff (as per Cartridge Weights) Mean [SD]	#Puffs/Cartridge	MMAD Mean [SD]	GSD Mean [SD]
3 seconds	2.4 [0.1]	180	1.0 [0.1]	1.7 [0.1]
5 seconds Original Config	5.2 [0.1]	120	1.4 [0.1]	1.7 [0.02]
5 seconds w/ Configuration Changes	4.9 [0.1]	130	1.1 [0.02]	1.5 [0.02]



- Adjustment of puff duration from 3 seconds to 5 seconds showed a marked increase in e-vapor product output but decreased the usable number of puffs per cartridge
- Particle size increased to 1.4 µm at the nose-port with 5 second puff durations. Configuration changes which included moving aerosol dilution air closer to the puff port, reduced the particle size to 1.1 µm.
- When increasing from 120 puffs/cartridge to 130 puffs/cartridge, the output per puff decreased from 5.1 to 4.9 mg/puff based on cartridge weight loss
- Achieved target concentration (1300 µg TPM/L) at the nose-port with RAM %RSD of ≤5% when using 130 puffs per cartridge

CONCLUSIONS

- Output from one smoke machine to multiple carousels was successfully accomplished with consistent gravimetric and constituent concentrations seen at the nose-port
- Aerosol particle size increased from 1.0 to 1.4 µm when puff duration was increased from 3 sec to 5 sec. With configuration changes including relocating aerosol dilution air closer to the puff port, the particle size decreased to 1.1 µm
- Target aerosol concentration at the nose-port with 130 puffs instead of 120 puffs per cartridge was achieved. Using 130 puffs per cartridge enables testing till further depletion of cartridge