Biomarkers of Combustion-Related Toxicants Decrease after Smokers Switch to an Electronic Cigarette

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Background

- Aerosol of e-cigarettes (EC) is much less complex than combustible cigarette smoke
- Limited work to assess biomarkers of exposure after a short-term switch from combustible cig to EC
- As a newly deemed product, ECs will require regulatory submission and authorization to be legally marketed
- ENDS PMTA Draft Guidance recommends inclusion of data related to biomarkers of exposure

Study Objective

- To evaluate biomarkers of exposure in smokers who switch to an EC or nicotine gum
  - Baseline period – 2 days of Usual Brand (UB) Cigarette
  - *Ad libitum* product switch period – 5 days of e-cigarette or nicotine gum
- After 5 days of product switch, assess changes in:
  - ✓ Biomarkers of tobacco exposure
  - ✓ Product use patterns
  - ✓ Nicotine pharmacokinetics
  - ✓ Urge to smoke

Study Participants

- Generally healthy males and females, 21-60 yrs
- Current, exclusive smoker of ≥10 cigarettes per day (CPD)
- Non-menthol and menthol smokers were included and randomized separately

Participant Randomization

Non-Menthol Smokers

VUSE Original

Nicotine Gum – 4 mg

Menthol Smokers

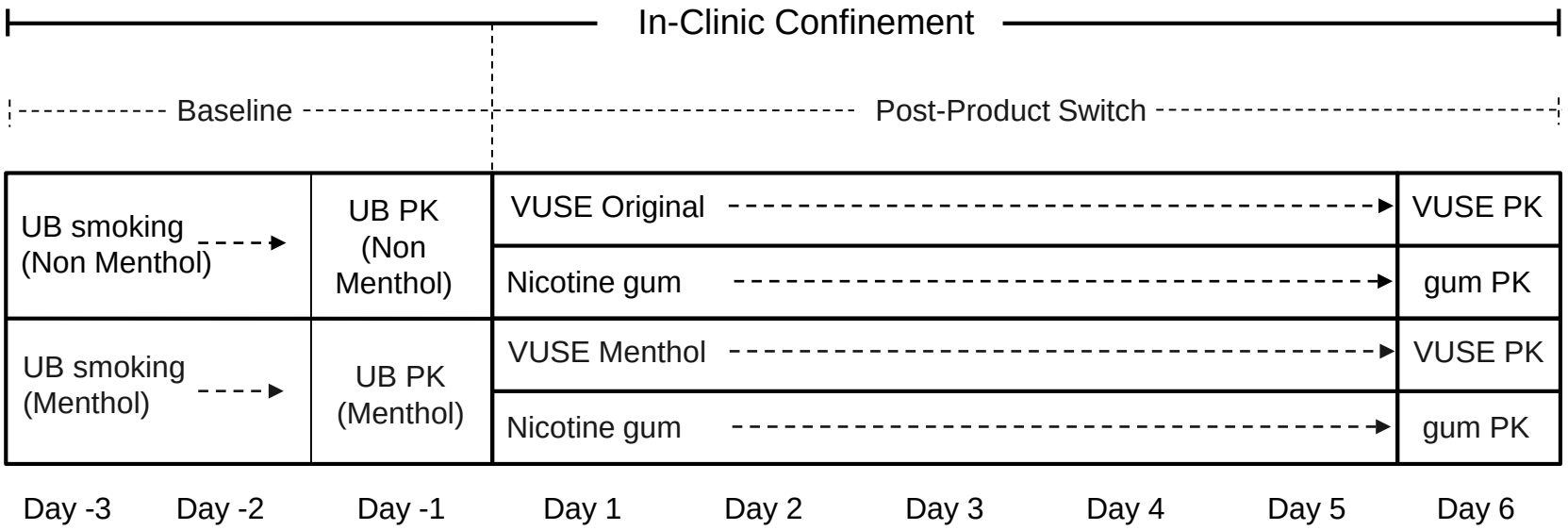
VUSE Menthol

Nicotine Gum – 4 mg

Clinical Conduct

- DaVita Clinical Research, Minneapolis, MN
  - January 2015 – May 2015
- 385 subjects screened
- 162 subject enrolled/158 subjects randomized
- 153 subjects completed
  - 37 subjects completed VUSE Original group (non-menthol smokers)
  - 38 subjects completed Nicotine gum group (non-menthol smokers)
  - 38 subjects completed VUSE Menthol group (menthol smokers)
  - 40 subjects completed Nicotine gum group (menthol smokers)

Study Design



Demographics and Baseline Characteristics

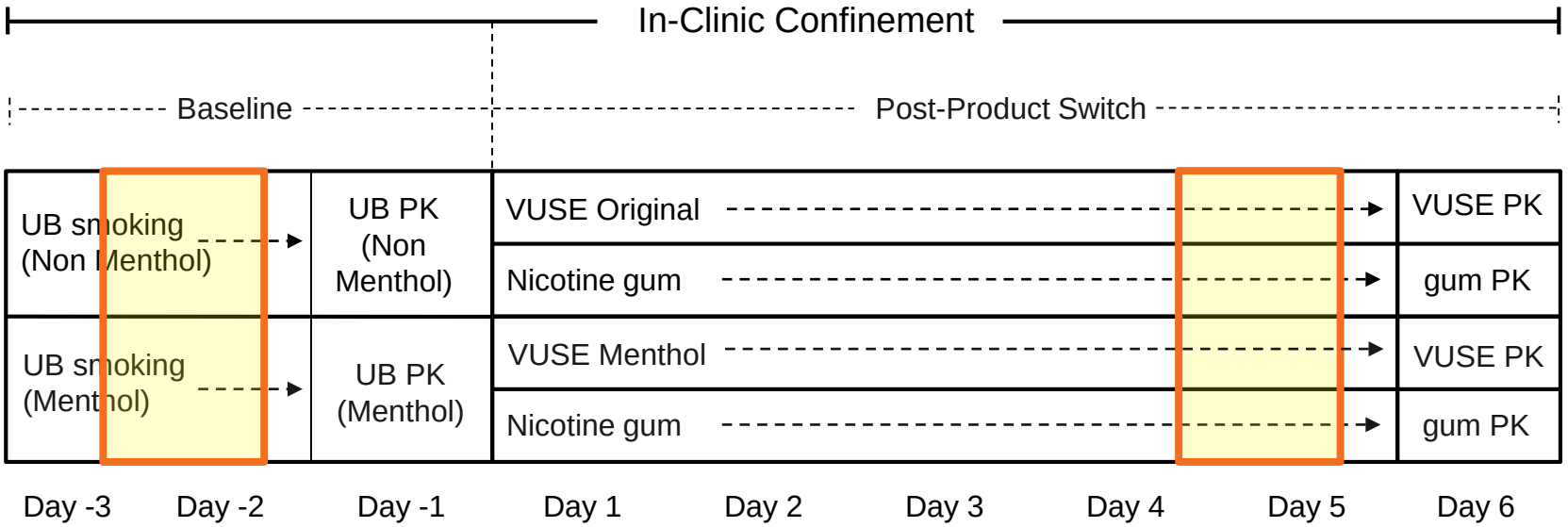
	NM Smoker – VUSE Original	NM Smoker – Gum	M Smoker – VUSE Menthol	M Smoker – Gum
Subjects (n)	38	39	40	41
Age (yr)	41.6	40.2	42.6	41.5
Female/Male (n)	11/27	14/25	15/25	11/30
Race (%)				
Black/African American	37%	33%	63%	71%
White	55%	64%	28%	15%
Other	8%	3%	10%	15%
FTCD	6.0	6.3	6.0	6.2
CPD	14.0	14.4	14.5	14.3

Adverse Events

	NM Smoker – VUSE Original	NM Smoker – Gum	M Smoker – VUSE Menthol	M Smoker – Gum
Subjects	38	39	40	41
Any AE	17	26	18	22
Possibly Related	5	8	6	7
Related	4	7	2	4
AE Causing Usage Discontinued	0	0	0	1
Most Common AE – Causally Related (n)	Cough (2)	Oropharyngeal pain (2)	Headache (4)	Dyspepsia (3)
Any SAE	0	0	0	0

Study Design

Biomarker Data Presented



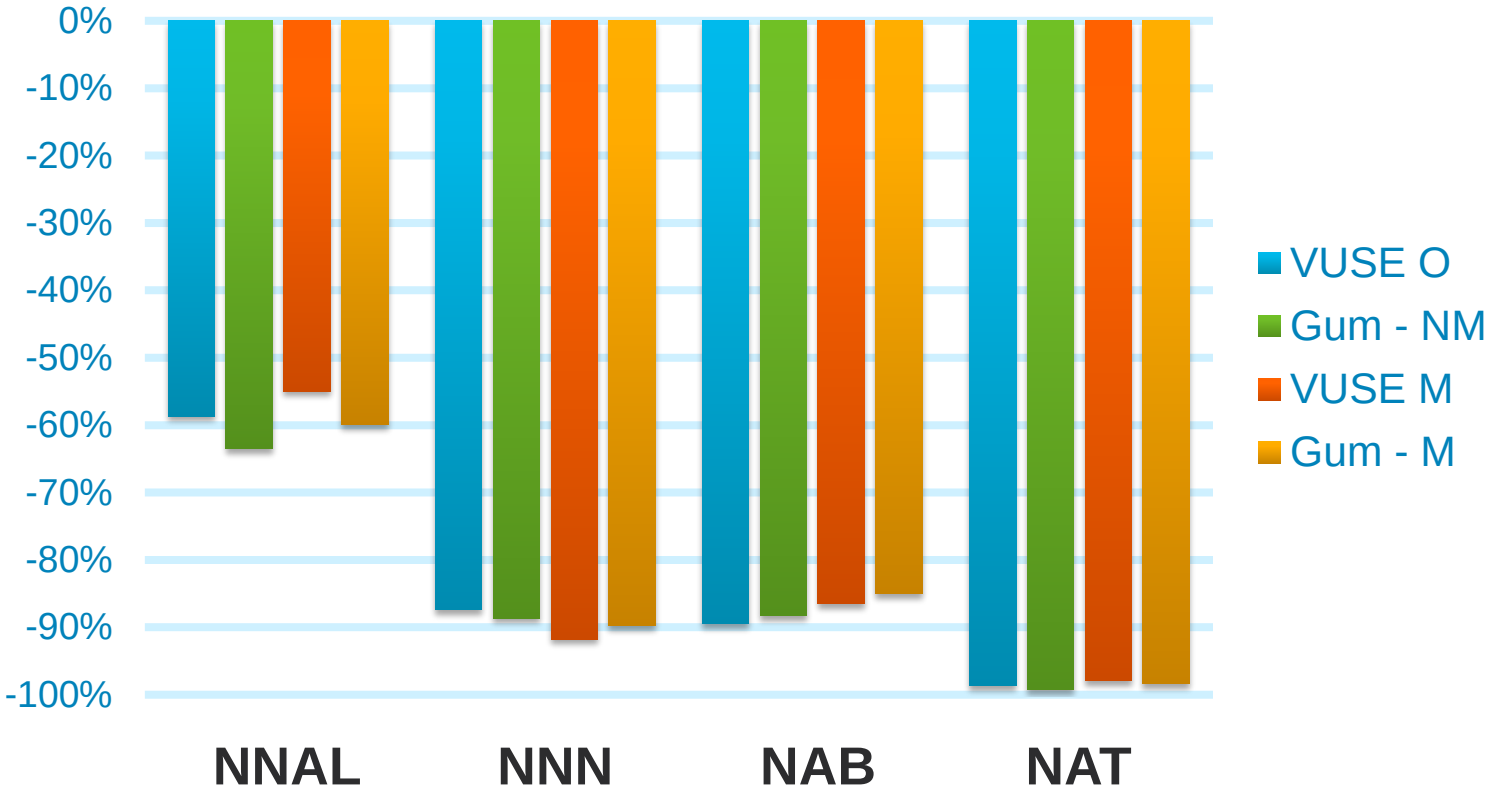
24h urine collected while smoking

24h urine collected post-product switch

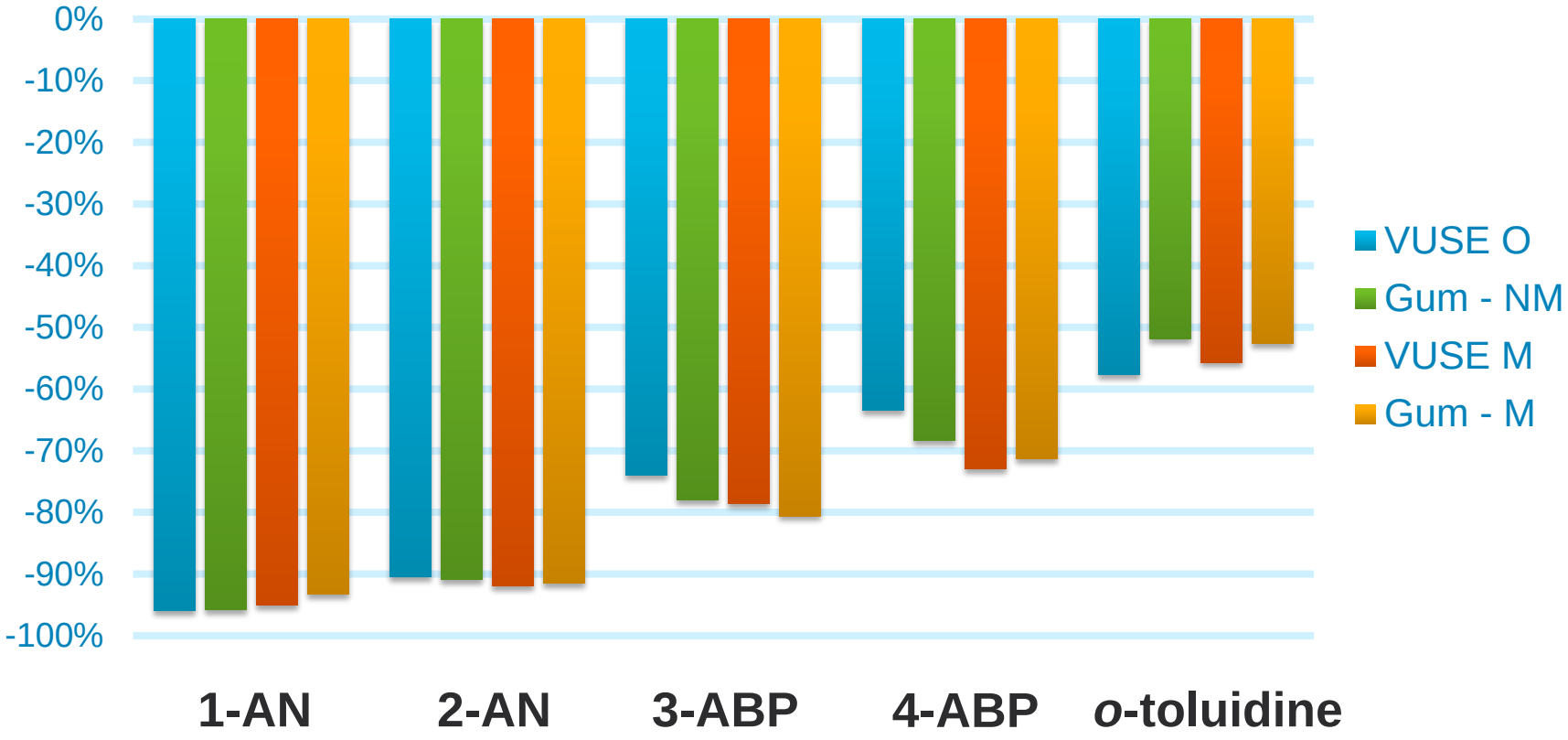
Constituents or Biomarkers Measured

- Tobacco Specific Nitrosamines
  - NNN
  - NNK (NNAL)
  - NAB
  - NAT
- Aromatic Amines
  - 1-aminonaphthalene
  - 2-aminonaphthalene
  - 3-aminobiphenyl
  - 4 aminobiphenyl
  - *o*-toluidine
- Polycyclic Aromatic Hydrocarbons
  - Naphthalene equivalents (1-OH- and 2-OH-naphthalene)
  - Fluorene (2-OH-fluorene)
  - B[a]P (3-OH-B[a]P)
  - Pyrene (1-OH-pyrene)
- Vapor Phase Constituents
  - Benzene (SPMA)
  - Acrolein (HPMA)
  - Crotonaldehyde (HMPMA)
  - Ethylene Oxide (HEMA)
  - Acrylonitrile (CEMA)
  - 1,3-butadiene (MHBMA)
  - Hydrogen cyanide (SCN)
  - Acrylamide equivalents (AAMA and GAMA)
  - COHb (Carbon Monoxide)
- Nicotine Equivalents
- Urine Mutagenicity

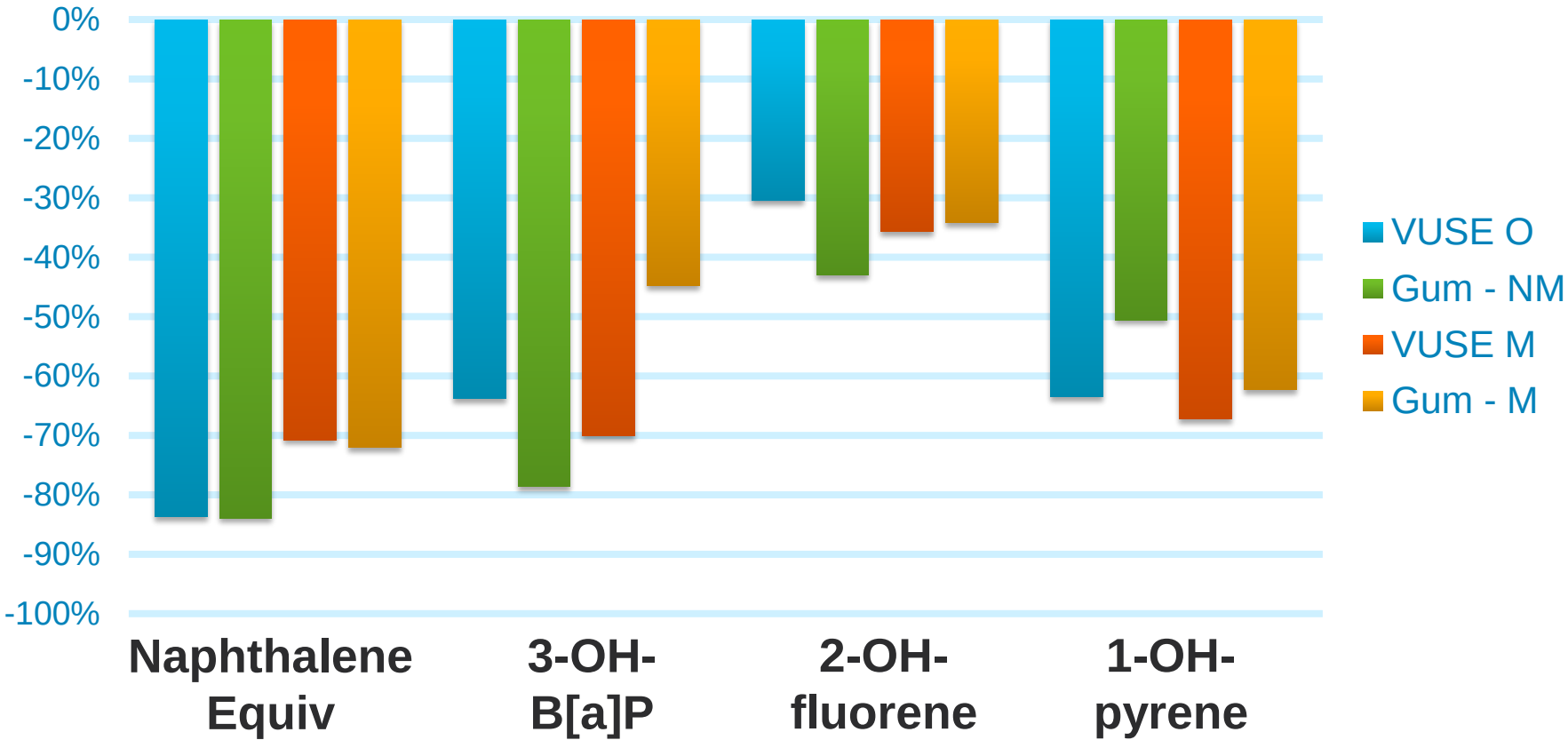
Change in TSNAs after 5-Day Switch



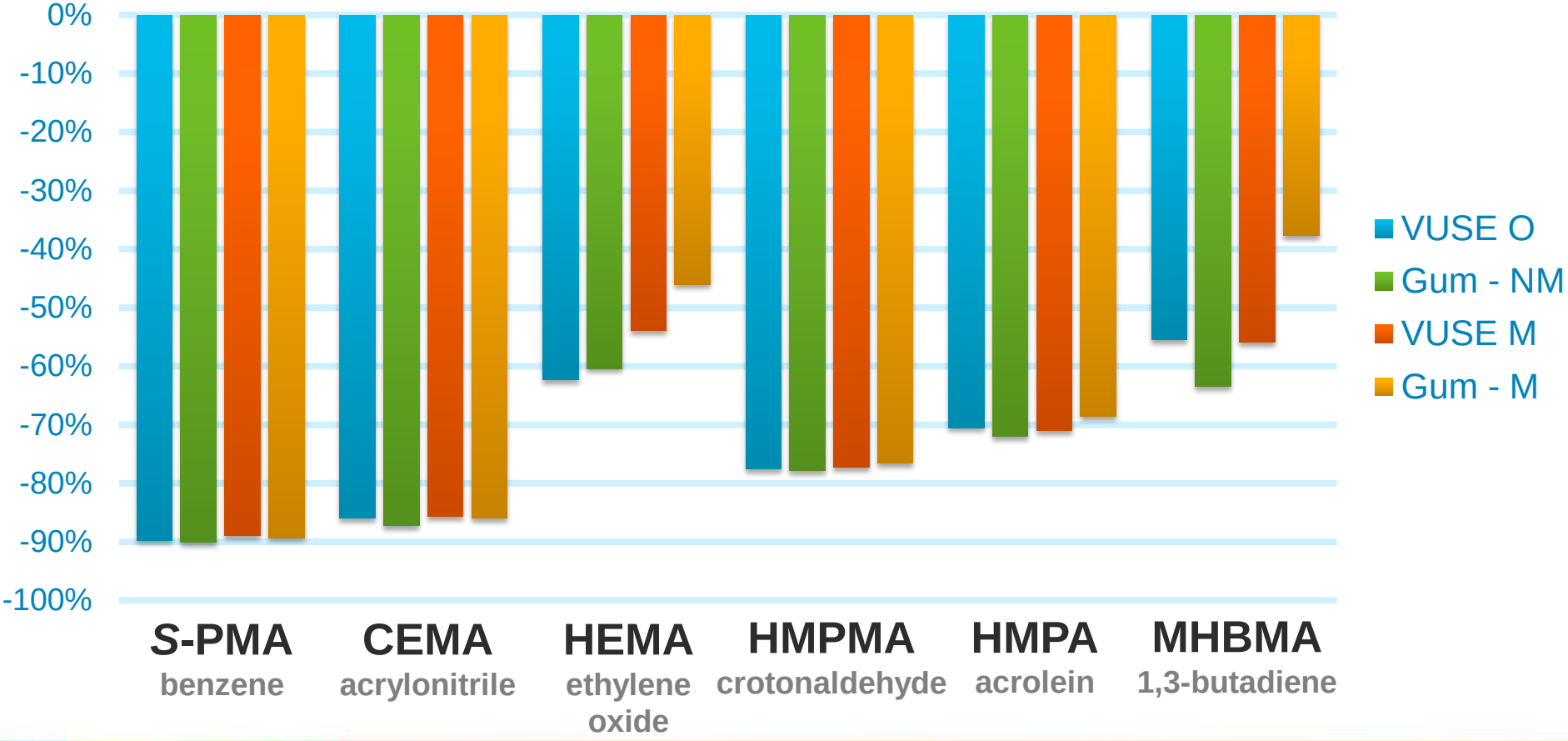
Change in Aromatic Amines after 5-Day Switch



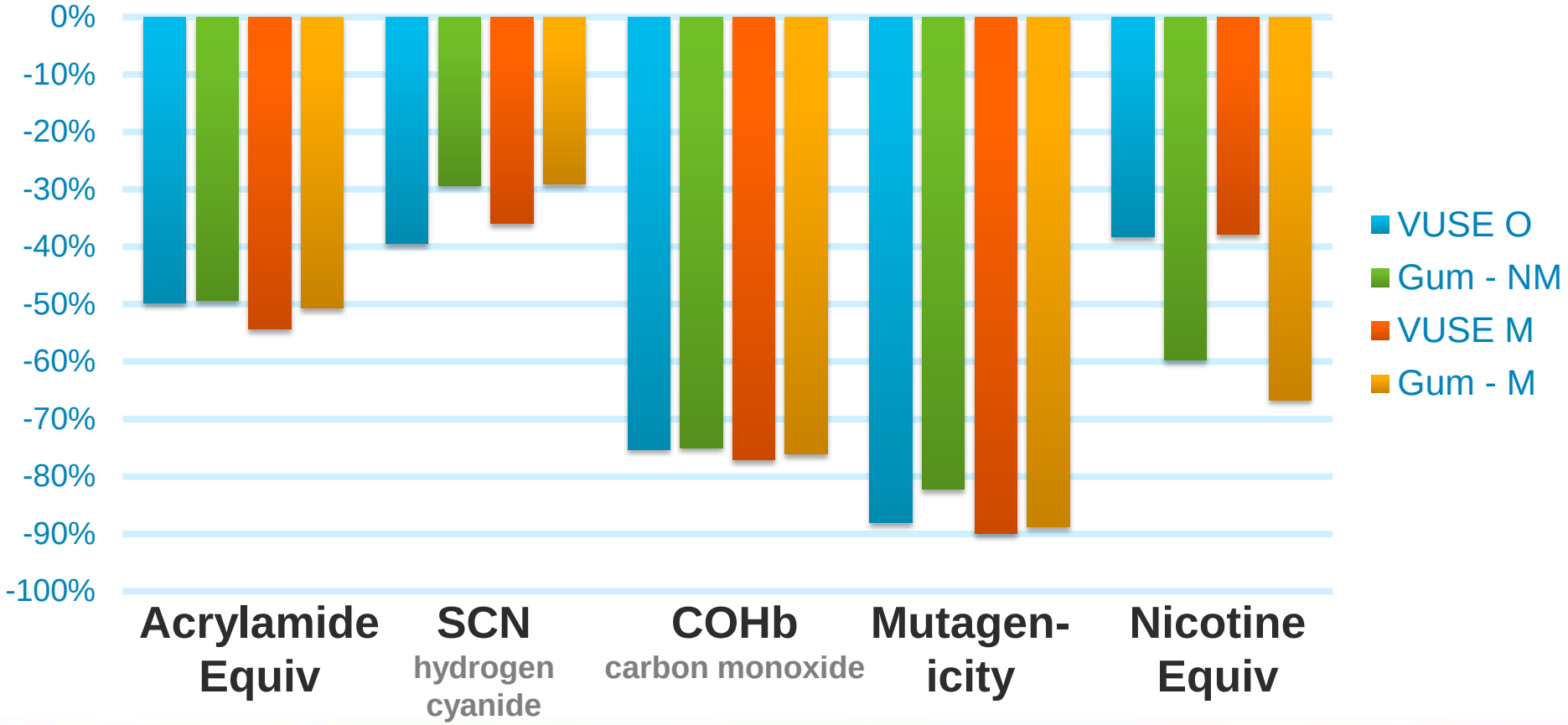
Change in PAHs after 5-Day Switch



Change in Vapor Phase Biomarkers after 5-Day Switch



Change in Biomarkers after 5-Day Switch

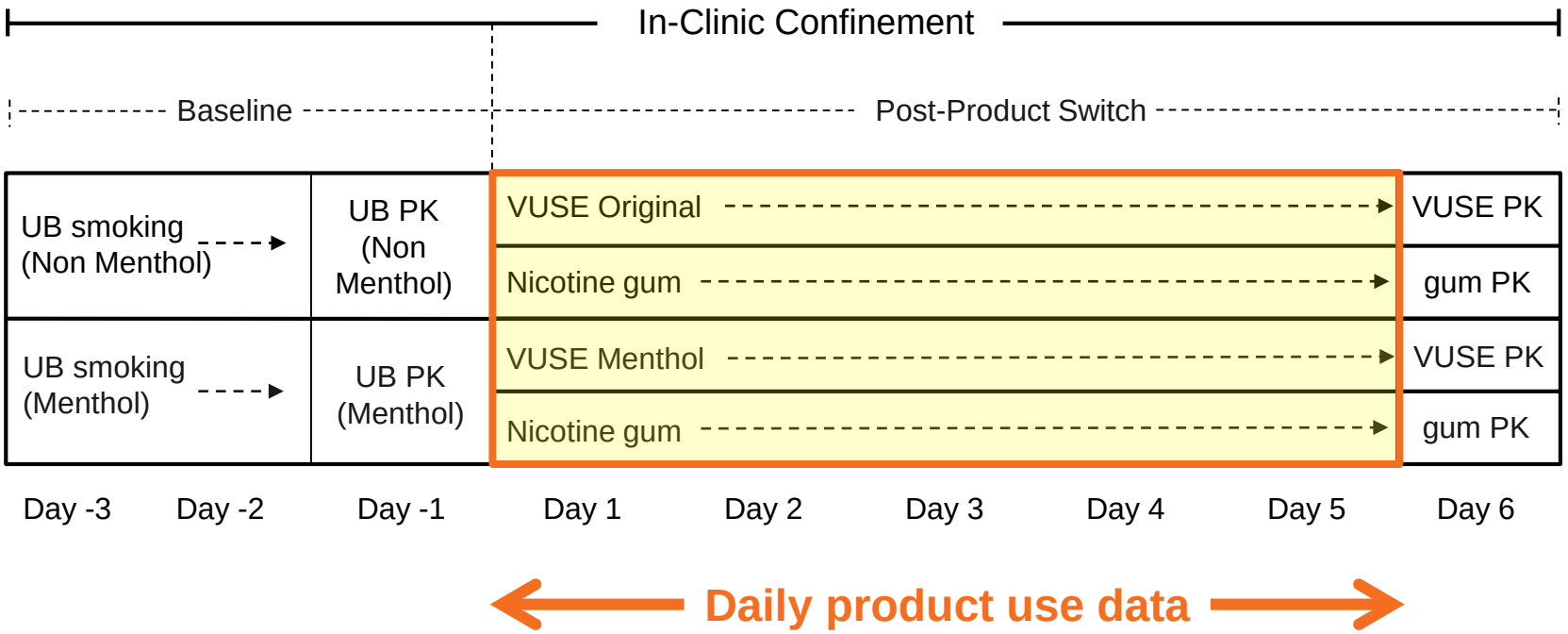


Observations – Biomarkers

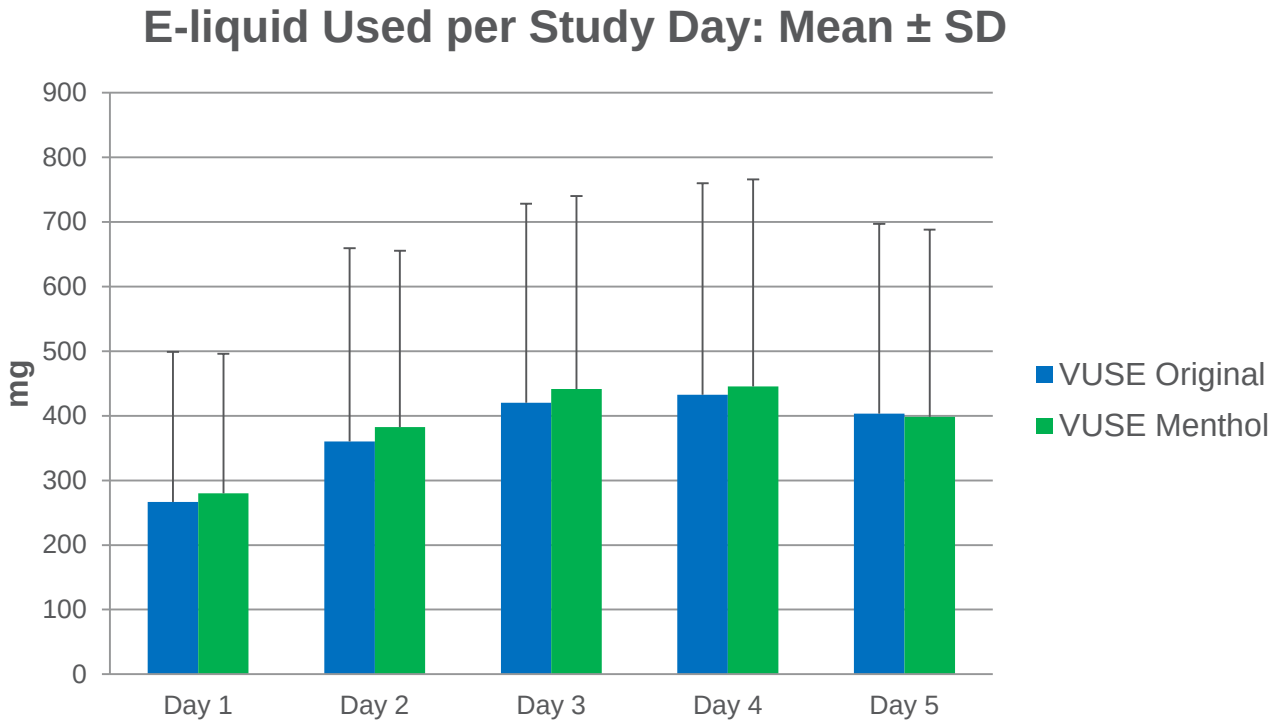
- Biomarker reductions in the EC cohorts are generally the same as the gum cohorts.
- Biomarkers are reduced ~30-99% in all cohorts.
  - MHBMA and 2-OH-fluorene reductions smaller than expected, but similar across all cohorts
  - 3-OH-BaP results driven by subjects with results BLQ at baseline
- Reductions are typically in agreement with reductions observed in abstinence groups in previous switching studies.

Study Design

Use Data Presented



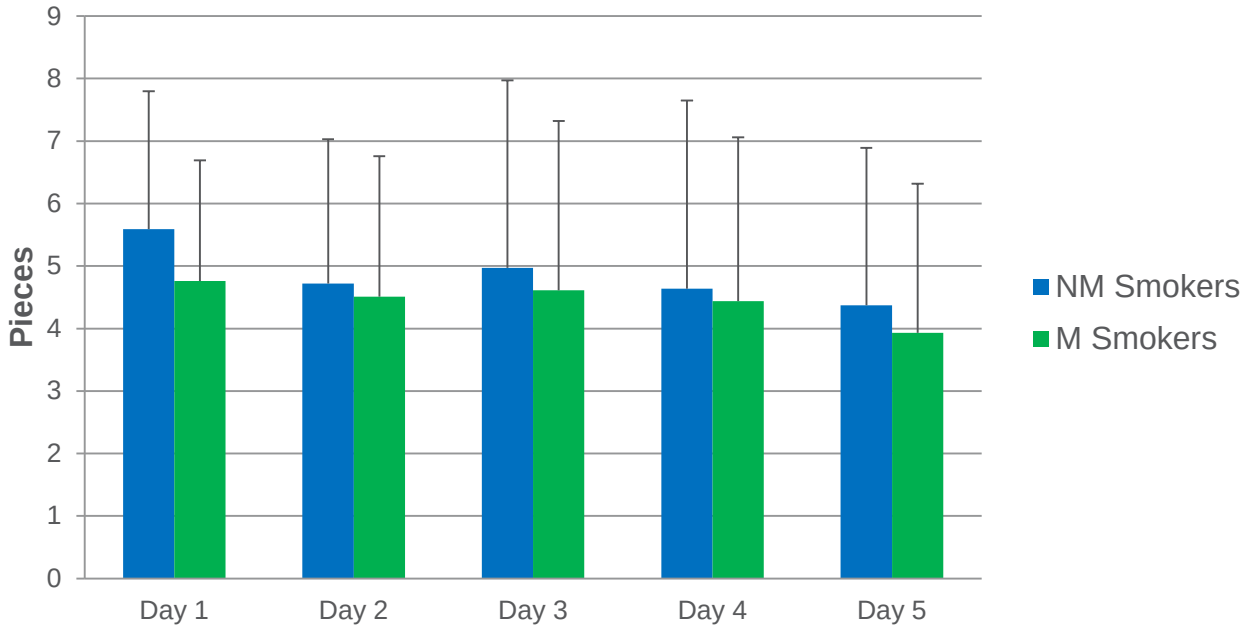
Product Use Results



- 57% increase in e-liquid consumption from Day 1 to Day 3

Product Use Results

Gum Used per Study Day: Mean ± SD



- Gum use relatively consistent across study days

Observations – Product use

- During short-term switch, e-liquid use increased 57% from Day 1 to Day 3.
- Suggests participants learn to use ECs within three days of switching.
- Gum use relatively consistent across study days.

Acknowledgements

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Thank You