

**An Open-label, Randomized,
Parallel Group, Controlled Study
to Evaluate Changes in
Biomarkers of Cigarette Smoke
Exposure and Biomarkers of
Potential Harm in Adult Smokers
Who Completely Switch to Using e-
Vapor Products for 24 Weeks**



Altria

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Primary Objective

Compare absolute changes in selected biomarkers from Baseline to End of Study between adult smokers who continue to smoke conventional cigarettes and adult smokers who have completely switched to the test e-vapor products for 24 weeks

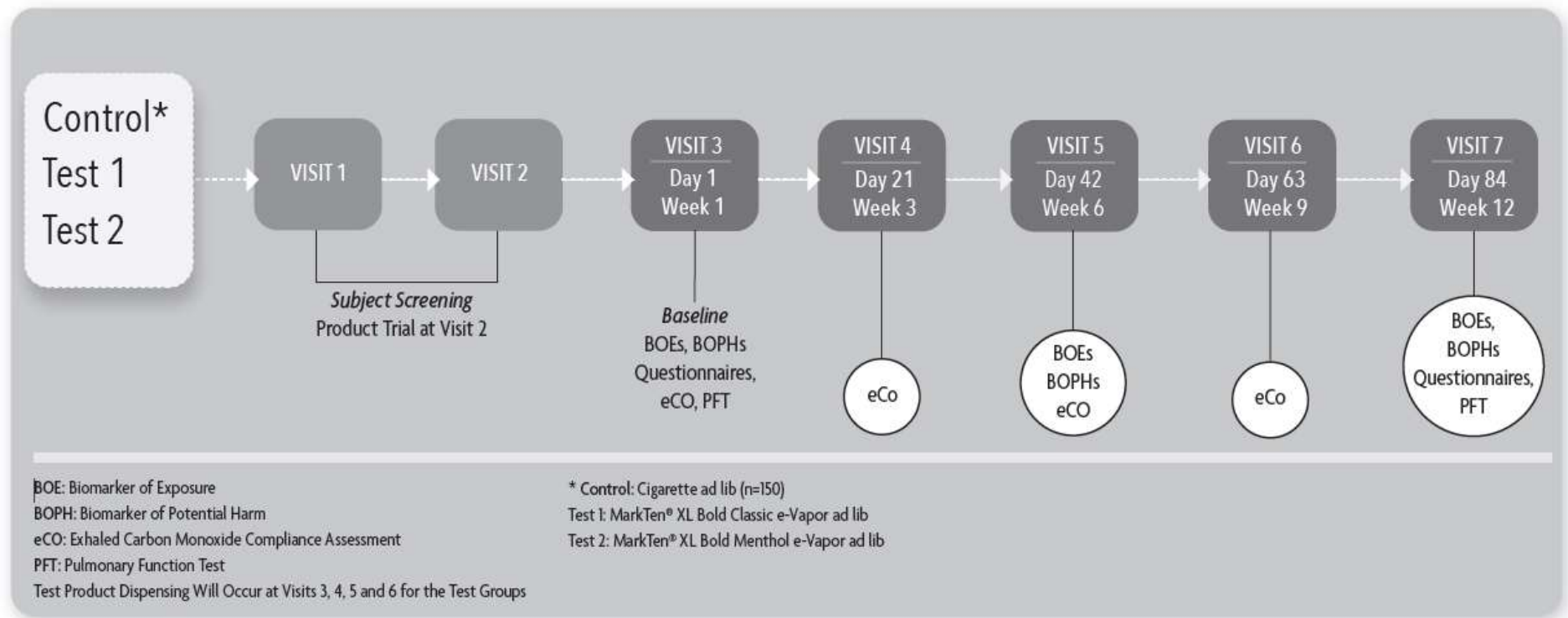
Study Products



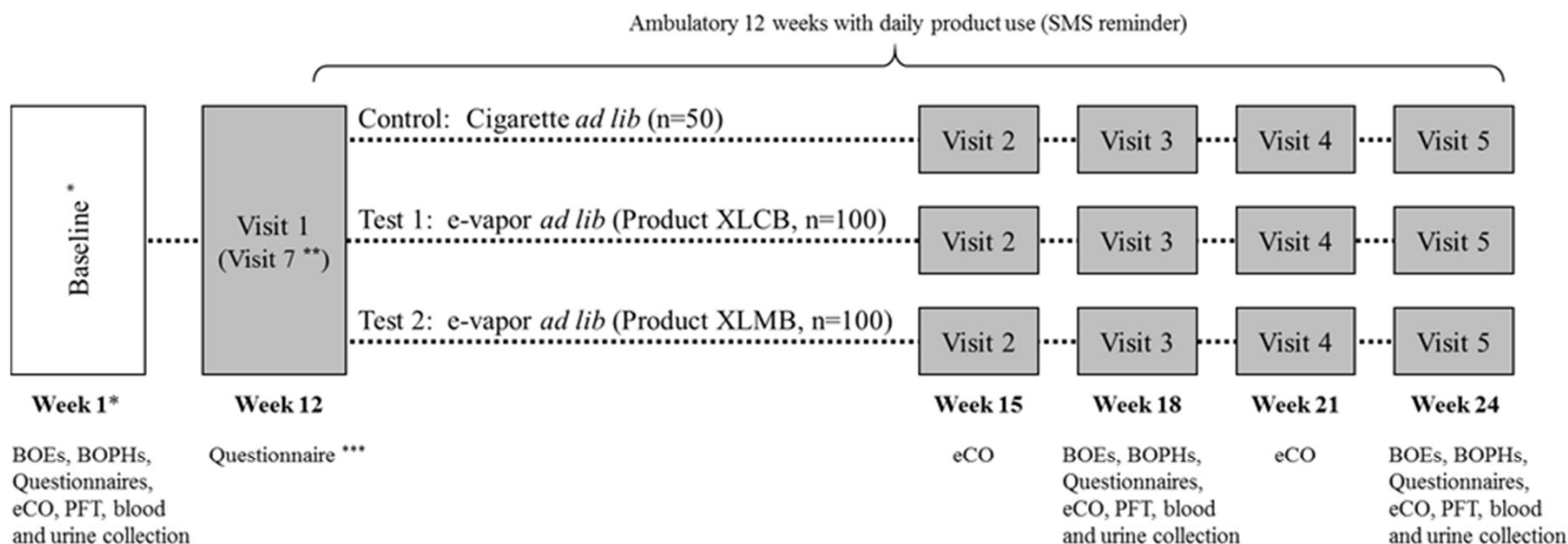
Product	Nicotine (% by weight)	Nicotine ^a (mg/puff)
Classic Bold	4.0	0.20
Menthol Bold	4.0	0.23

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

12 Week e-Vapor Switching Study



24 Week e-Vapor Switching Study



BOE: Biomarker of Exposure

BOPH: Biomarker of Potential Harm

eCO: Exhaled Carbon Monoxide compliance assessment

SMS: Short Message System

PFT: Pulmonary Function Test

* Baseline values reported on Day 1 (Week 1) or at Screening (for PFT only) of the 12-week ALCS-RA-16-06-EV study (CA20130) will be used.

** Visit 1 is the same as Visit 7 of the 12-week ALCS-RA-16-06-EV study (CA20130).

*** Changes in Your Health and Well-Being Questionnaire.

Test Products dispensing will occur at Visits 1, 2, 3, and 4 for the Test groups.



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Key Measurements

Biomarkers of Exposure (BOE)		
Biomarker	Constituent	FDA Classification
Total NNAL	NNK	Carcinogen
Carboxyhemoglobin (COHb)	Carbon Monoxide	Reproductive or Developmental Toxicant
Nicotine Equivalents (nicotine and 5 metabolites)	Nicotine	Reproductive or Developmental Toxicant, Addictive

Biomarkers of Potential Harm (BOPH)	
Biomarker	Indication
White Blood Cells (WBC)	Inflammation
High-density lipoprotein cholesterol (HDL-C)	Cardiovascular Risk
8-Epi-prostaglandin F2α (8-epi-PG F2α)	Oxidative Stress
11-Dehydrothromboxane B2 (11-DTX B2)	Platelet Activation
Soluble intercellular adhesion molecule-1 (sICAM-1)	Endothelial Function



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24 Week Study Subject: Demographics

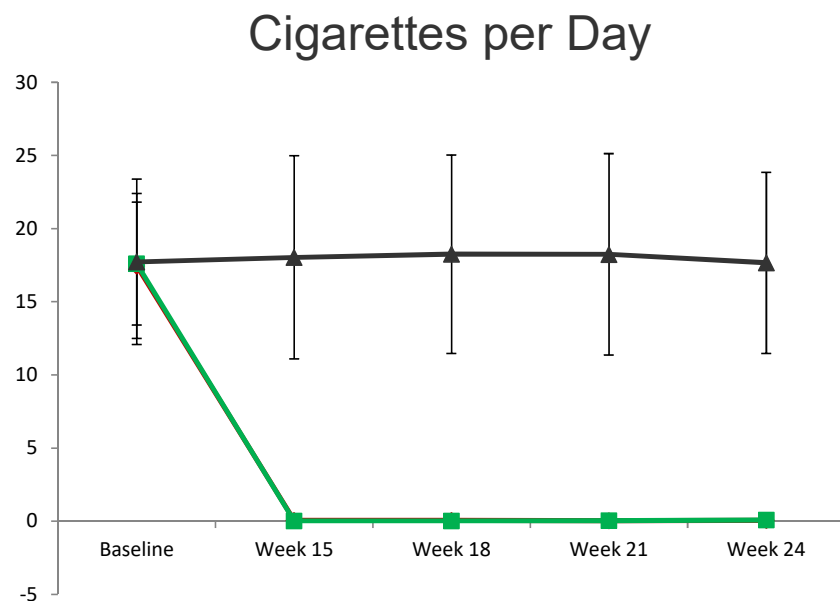
Trait	Category/Statistics	Classic Bold (n=48)	Menthol Bold (n=50)	Control (n=52)	Overall (n=150)
Gender	Female	23 (48%)	26 (52%)	27 (52%)	76 (51%)
	Male	25 (52%)	24 (48%)	25 (48%)	74 (49%)
Race	Other	1 (0%)	1 (2%)	0 (0%)	2 (2%)
	Black or African American	9 (19%)	5 (10%)	12 (23%)	26 (17%)
	White/Caucasian	38 (79%)	44 (88%)	40 (77%)	122 (81%)
Age (yrs)	Mean	43.2	44.4	45.6	44.4
	SD	8.36	10.80	9.86	9.73
BMI (kg/m ²)	Mean	28.258	28.262	28.560	28.364
	SD	5.1134	5.2222	4.9523	5.0627

24 Week Study: Tobacco History

		Classic Bold	Menthol Bold	Control	Overall
	n	48	50	52	150
Cigarettes per Day	Mean	17.4	17.6	17.7	17.6
	SD	4.95	4.20	5.65	4.95
Years Smoked	Mean	21.7	25.9	26.5	24.7
	SD	7.90	10.59	11.19	10.19



24Week Study: Product Use



◆ Classic Bold
■ Menthol Bold
▲ Control

Average Cartridges per Day		
Group		Week 24
Classic Bold	N	47
	Mean	1.65
	SD	0.93
Menthol Bold	N	50
	Mean	1.48
	SD	0.78

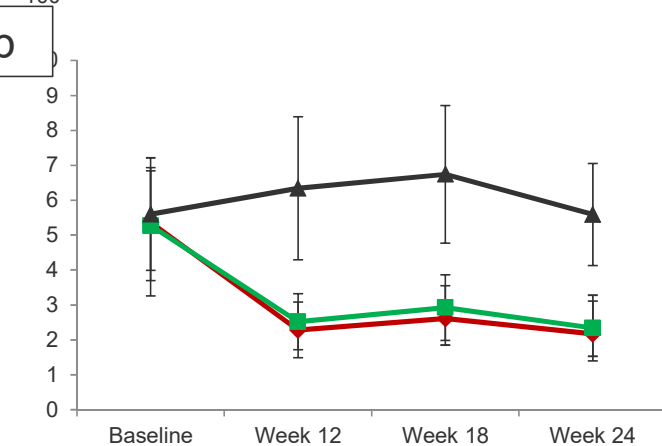
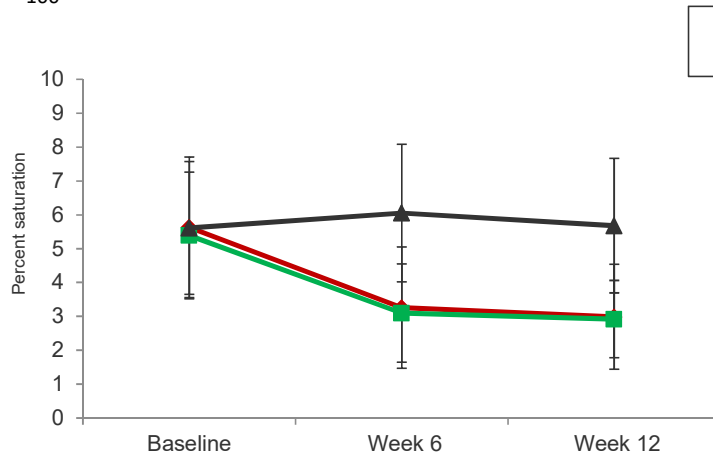
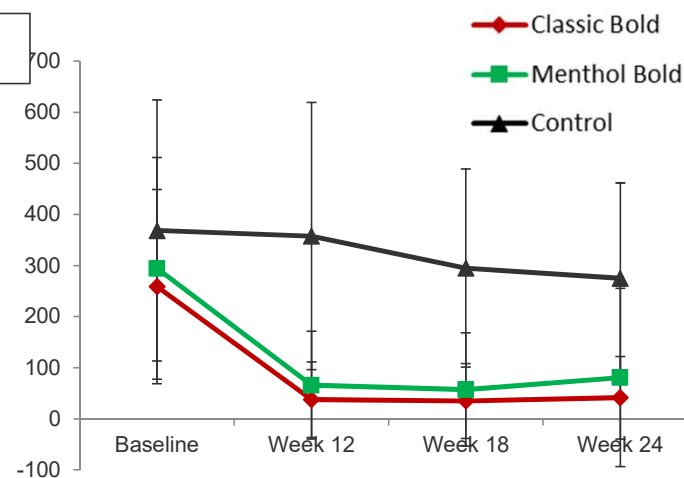
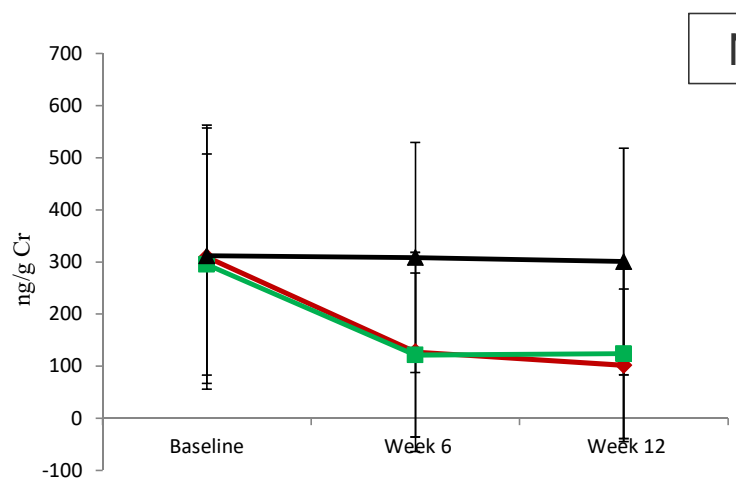
Arithmetic Means \pm SD

24 Week Study: Compliance

Group	Week	N	eCO Category n (%)		
			≤5	>5 - ≤8	>8
Classic Bold	12	47	46 (98)	1 (2)	0 (0)
	15	44	41 (93)	2 (5)	1 (2)
	18	41	38 (93)	2 (5)	1 (2)
	21	42	35 (83)	5 (12)	2 (5)
	24	42	35 (83)	5 (12)	2 (5)
Menthol Bold	12	50	43 (86)	7 (14)	0 (0)
	15	49	40 (82)	6 (12)	3 (6)
	18	49	44 (90)	3 (6)	2 (4)
	21	46	39 (85)	5 (11)	2 (4)
	24	48	40 (83)	4 (8)	4 (8)



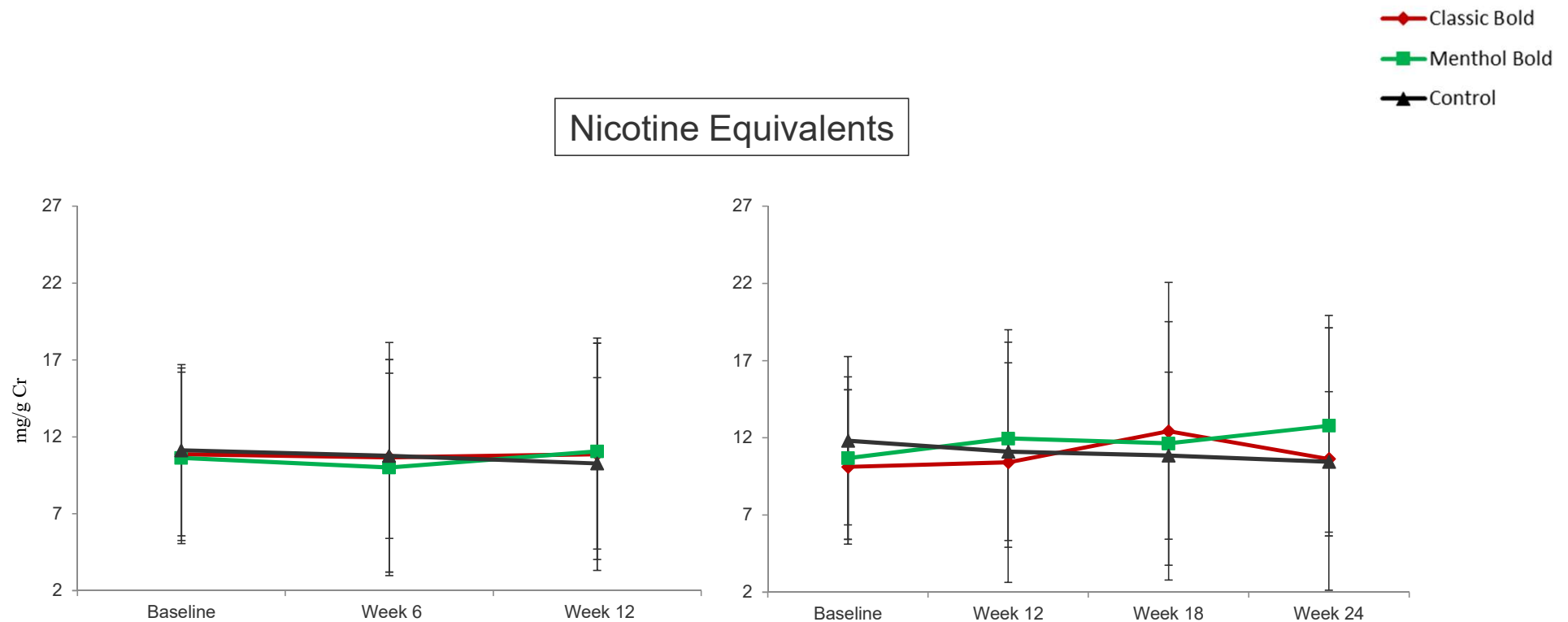
Biomarkers of Exposure



Arithmetic Means \pm SD

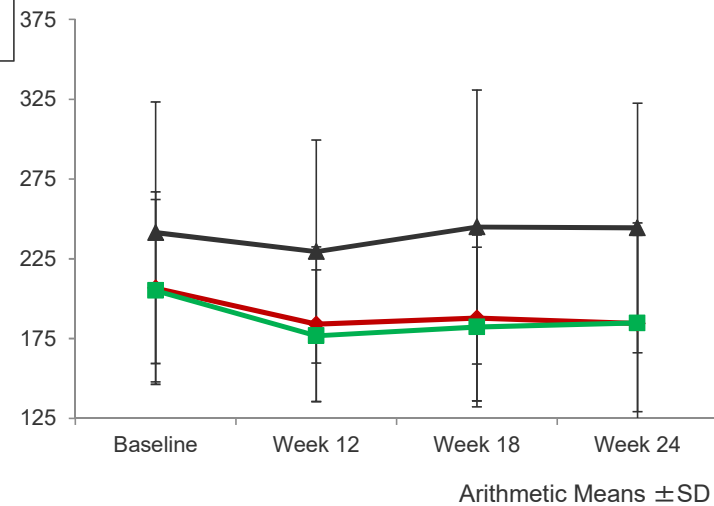
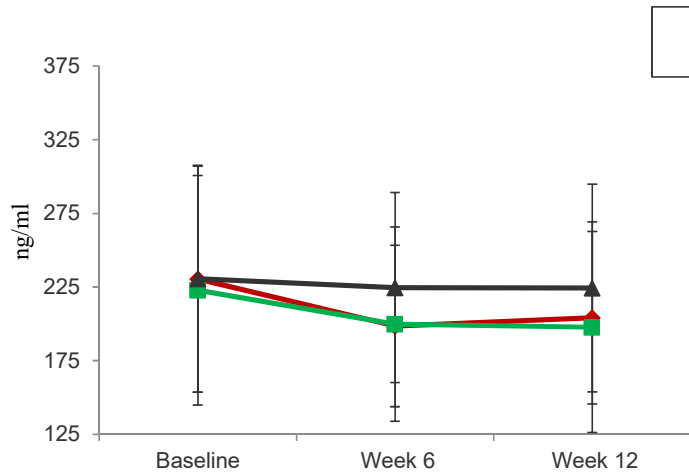
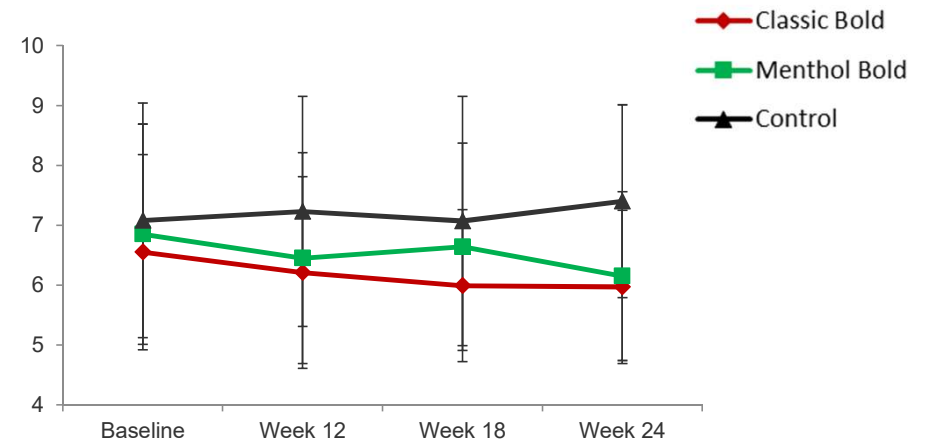
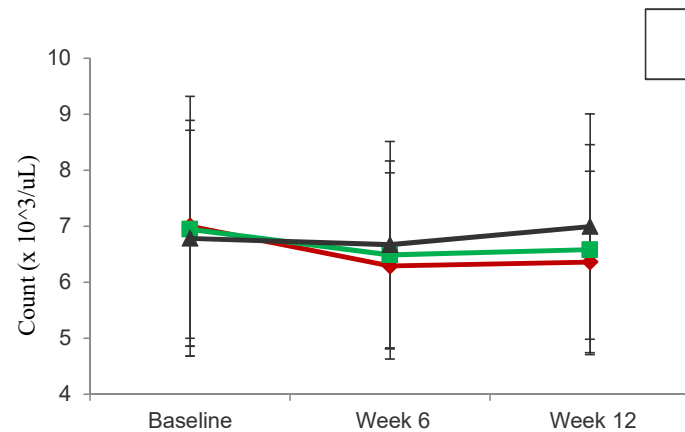
Biomarkers of Exposure

Nicotine Equivalents

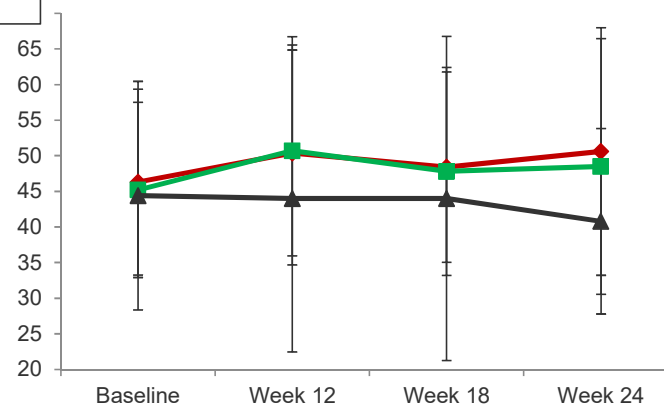
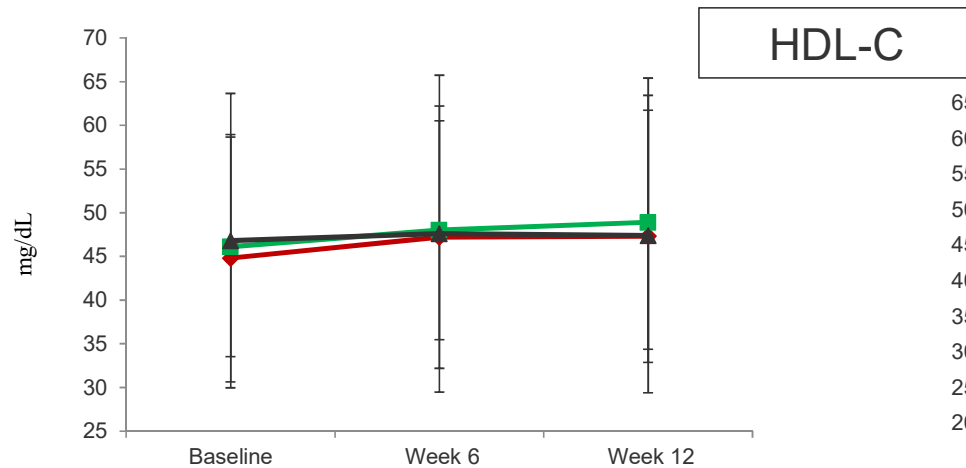
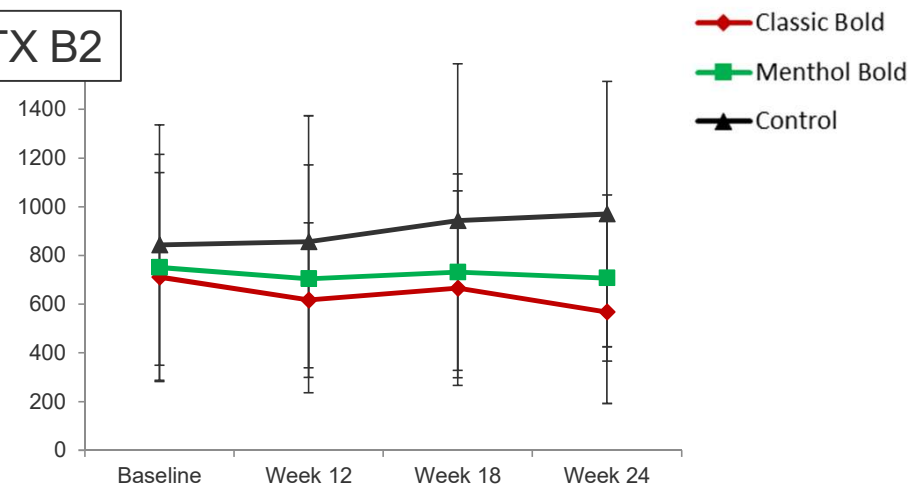
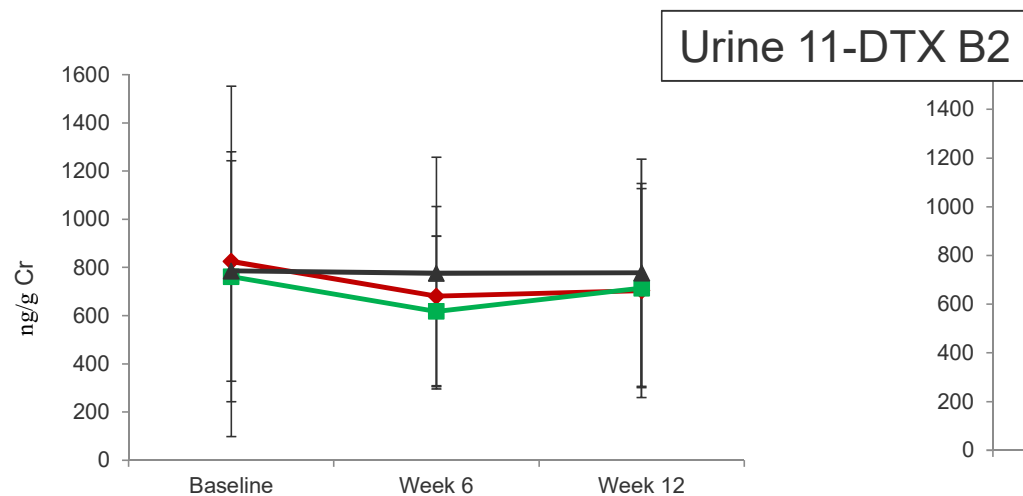


Arithmetic Means \pm SD

Biomarkers of Potential Harm



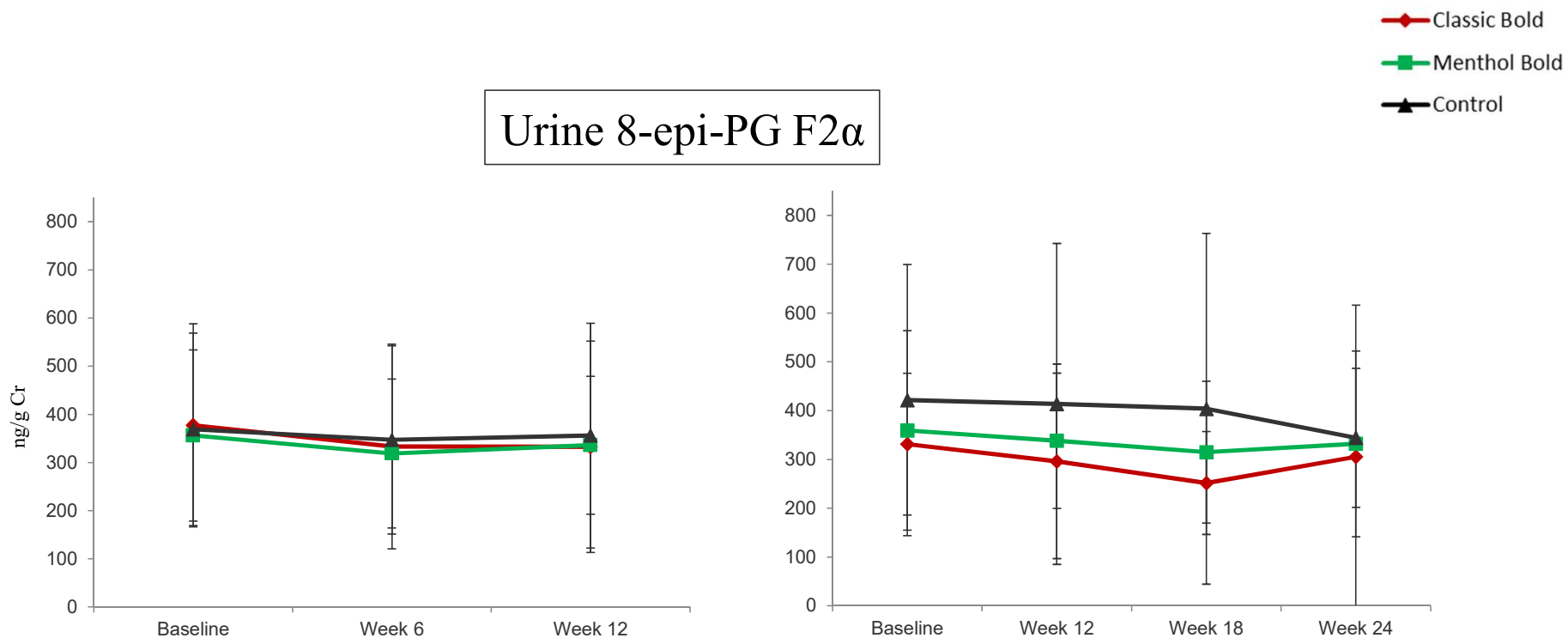
Biomarkers of Potential Harm



Arithmetic Means \pm SD

Biomarkers of Potential Harm

Urine 8-epi-PG F2 α



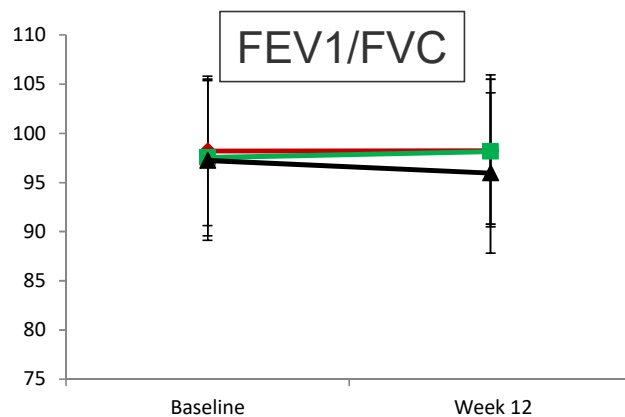
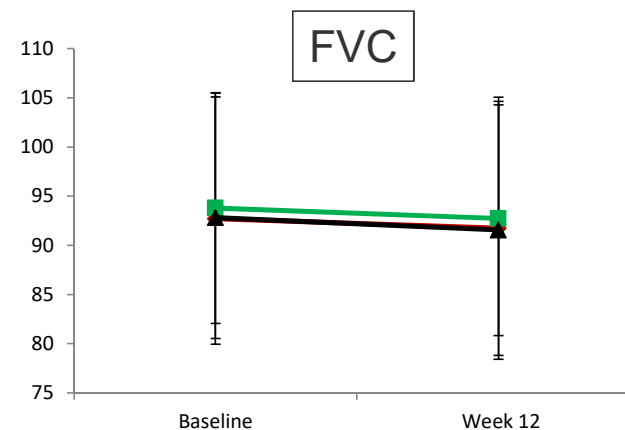
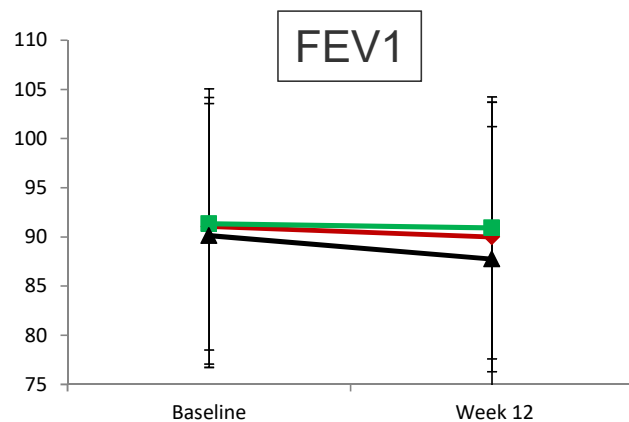
12 Week Study: Biomarkers of Potential Harm

Biomarker	Absolute Change from Baseline to 12 Weeks				
	LS Means			LS Mean Difference (Test - Control)	p-value^
	Group	Test (n)	Control (n)		
Whole Blood WBC Count (x 10 ³ /uL)	Classic Bold	-0.686 (110)	0.111 (128)	-0.797	0.0002
	Menthol Bold	-0.342 (119)	0.111 (128)	-0.453	0.0639
Urine 11-DTX B2 (ng/g Cr)	Classic Bold	-74.904 (110)	-2.635 (125)	-72.269	0.4543
	Menthol Bold	-62.755 (120)	-2.635 (125)	-60.120	0.6061
Plasma sICAM-1 (ng/mL)	Classic Bold	-25.921 (111)	-5.902 (129)	-20.019	0.0005
	Menthol Bold	-26.899 (120)	-5.902 (129)	-20.997	0.0002
Serum HDL-C (mg/dL)	Classic Bold	3.468 (110)	1.778 (128)	1.690	0.3934
	Menthol Bold	3.329 (119)	1.778 (128)	1.552	0.4576
Urine 8-epi-PG F2 α (ng/g Cr)	Classic Bold	-31.350 (111)	-4.759 (128)	-26.591	0.5234
	Menthol Bold	-18.096 (120)	-4.759 (128)	-13.337	0.9331

24 Week Study: Biomarkers of Potential Harm

Absolute Change From Baseline to Week 24					
Biomarker	LS Means				
	Group	Test (n)	Control (n)	LS Mean Difference (Test - Control)	p-value
WBC Count (x 10 ³ /uL)	Classic Bold	-0.90 (42)	0.24 (44)	-1.14	<.0001
	Menthol Bold	-0.85 (47)	0.24 (44)	-1.09	<.0001
Urine 11-DTX B2 (ng/g Cr)	Classic Bold	-169.74 (42)	182.63 (43)	-352.37	0.0002
	Menthol Bold	-53.57 (48)	182.63 (43)	-236.2	0.0242
Plasma sICAM-1 (ng/mL)	Classic Bold	-31.51 (42)	12.45 (44)	-43.97	0.0005
	Menthol Bold	-28.60 (47)	12.45 (44)	-41.05	0.0011
HDL-C (mg/dL)	Classic Bold	5.54 (41)	0.67 (44)	4.86	0.1422
	Menthol Bold	4.69 (46)	0.67 (44)	4.01	0.2841
Urine 8-epi-PG F2 α (ng/g Cr)	Classic Bold	-37.31 (42)	7.58 (44)	-44.89	0.9026
	Menthol Bold	-28.97 (48)	7.58 (44)	-36.56	0.9578

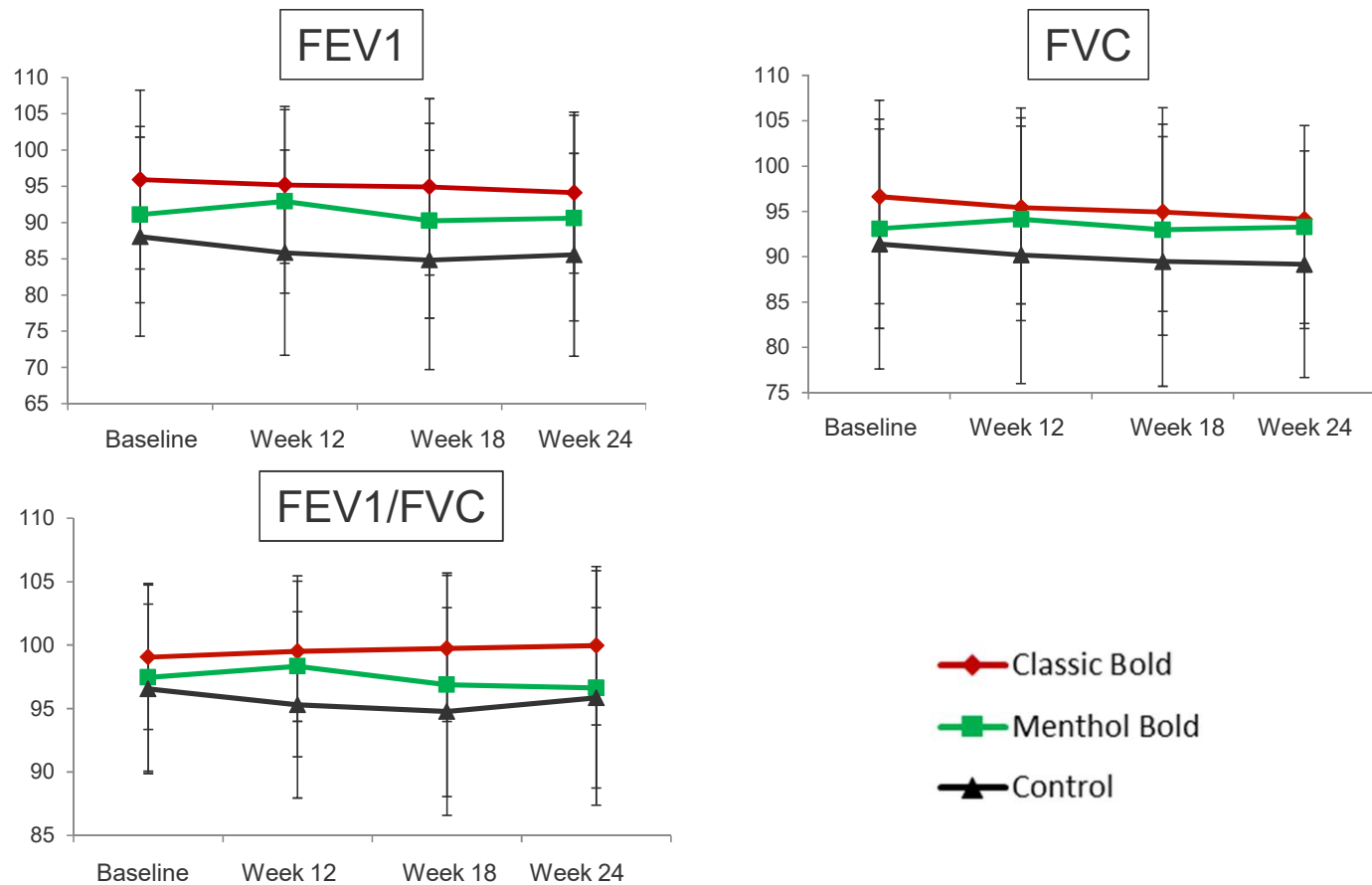
12 Week Study: Spirometry (percent predicted)



—◆— Classic Bold
—■— Menthol Bold
—▲— Control

Arithmetic Means \pm SD

24 Week Study: Spirometry (percent predicted)



Arithmetic Means \pm SD

24 Week Study: Spirometry (percent predicted)

	Absolute Change From Baseline to Week 24				
	LS Means				
Pulmonary Function Parameter	Comparison	Test(n)	Control(n)	LS Mean Difference (Test - Control)	p-value
Percent of Predicted FEV1 (%)	Classic Bold	-1.32 (36)	-3.88 (39)	2.56	0.0648
	Menthol Bold	-0.48 (40)	-3.88 (39)	3.40	0.0106
Percent of Predicted FVC (%)	Classic Bold	-1.76 (36)	-3.06 (39)	1.30	0.2799
	Menthol Bold	-0.25 (40)	-3.06 (39)	2.81	0.0155
Percent of Predicted FEV1/FVC (%)	Classic Bold	0.66 (36)	-1.30 (39)	1.96	0.0577
	Menthol Bold	-0.38 (40)	-1.30 (39)	0.92	0.3561

Overall Summary

Subjects switching to MarkTen[®] products demonstrated:

- High level of compliance with switching to MarkTen[®]
- Significant reduction in BOE (NNAL & COHb)
 - Nicotine exposure remained the same as for cigarettes
- Favorable changes in BOPH
 - WBC, Urine 11-DTX B2 and sICAM significantly reduced ($p < 0.0242$)
 - HDL and 8-epi all showed favorable changes
 - Favorable changes in lung function

Comparable outcomes were observed between the Menthol and Classic Bold MarkTen[®] products

Conclusions

- Complete switching from cigarettes to MarkTen[®] reduces exposure to smoke constituents and may reduce the risks of smoking related diseases
- Flavor does not appear to have an impact on the BOEs or BOPHs
- A 12-week study with the currently available biomarkers along with exclusive use should be sufficient enough to assess the potential health effects of a new tobacco product

תודה
Dankie Gracias
Спасибо شكراً
Merci Takk
Köszönjük Terima kasih
Grazie Dziękujemy Děkojame
Ďakujeme Vielen Dank Paldies
Kiitos Tänname teid 谢谢
Thank You Tak
感謝您 Obrigado Teşekkür Ederiz
감사합니다
Σας ευχαριστούμε
Bedankt Děkujeme vám
ありがとうございます
Tack

Presentation available at: www.altria.com/alcs-science



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