



Toxic and carcinogenic constituents in dissolvable tobacco products

**TPSAC Meeting
January 18-20, 2012**

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Dissolvable tobacco products

Star Scientific (2001)



RJ Reynolds (2008)

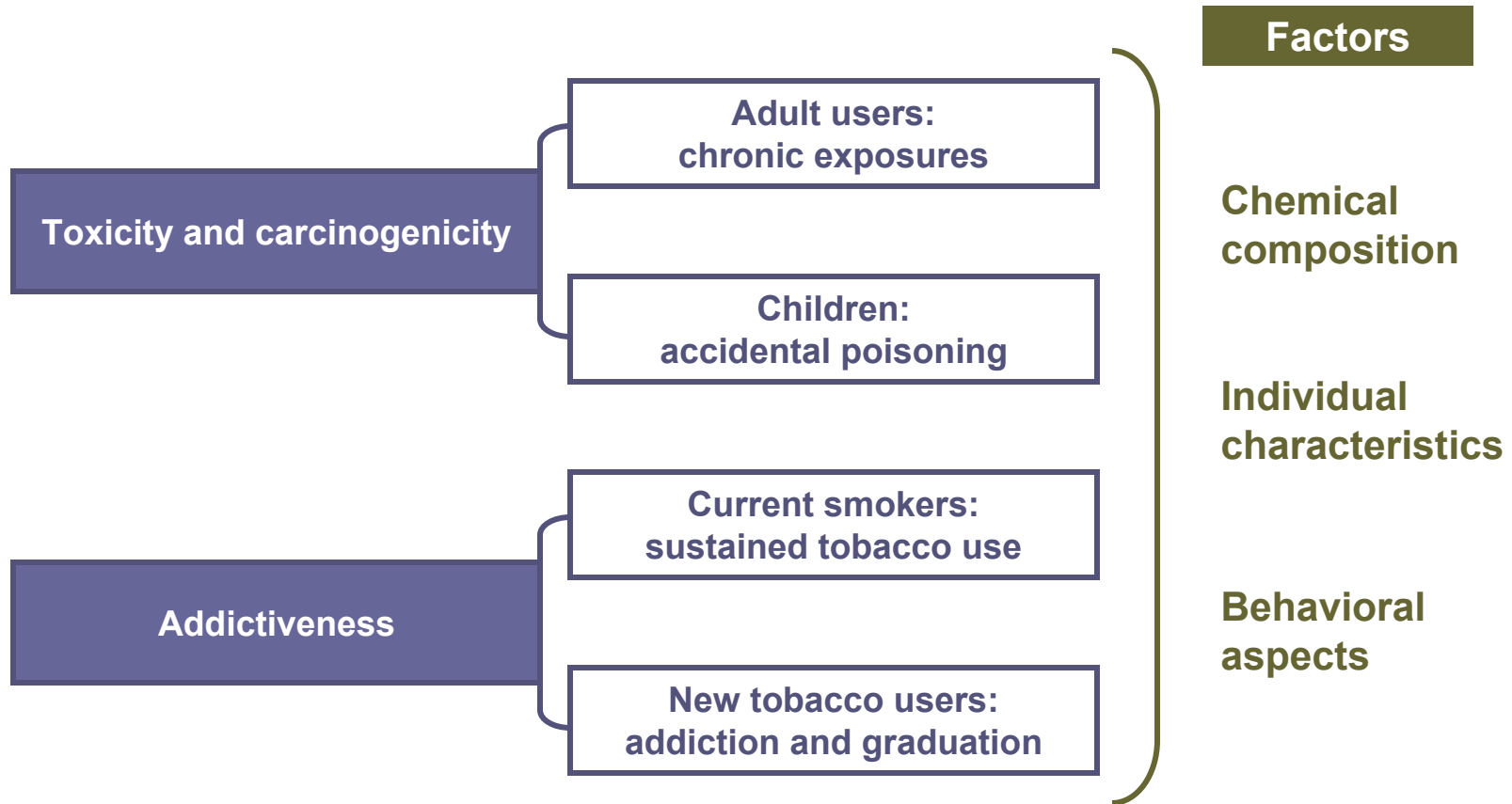


Philip Morris (2011)



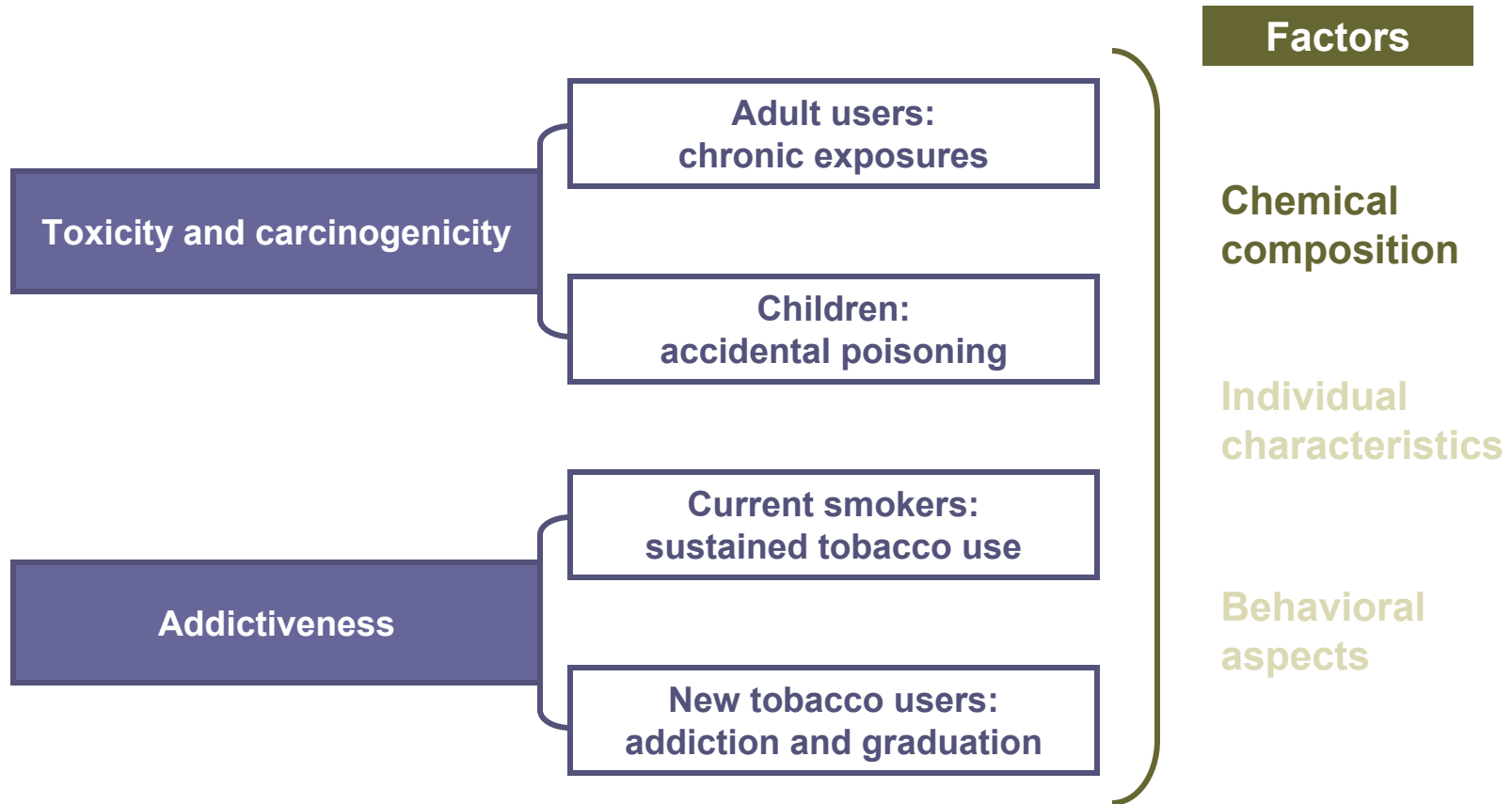


Some major concerns related to the use of dissolvable tobacco products





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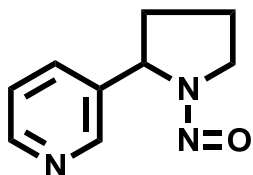




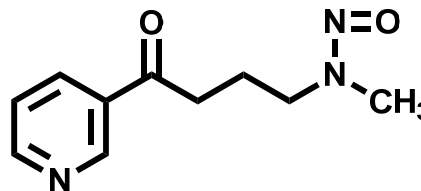
Constituents/characteristics analyzed in our laboratory

- Tobacco-specific *N*-nitrosamines
- Polycyclic aromatic hydrocarbons
- Nicotine, pH, and unprotonated nicotine
- Moisture content and portion weight

Tobacco-Specific *N*-Nitrosamines (TSNA)



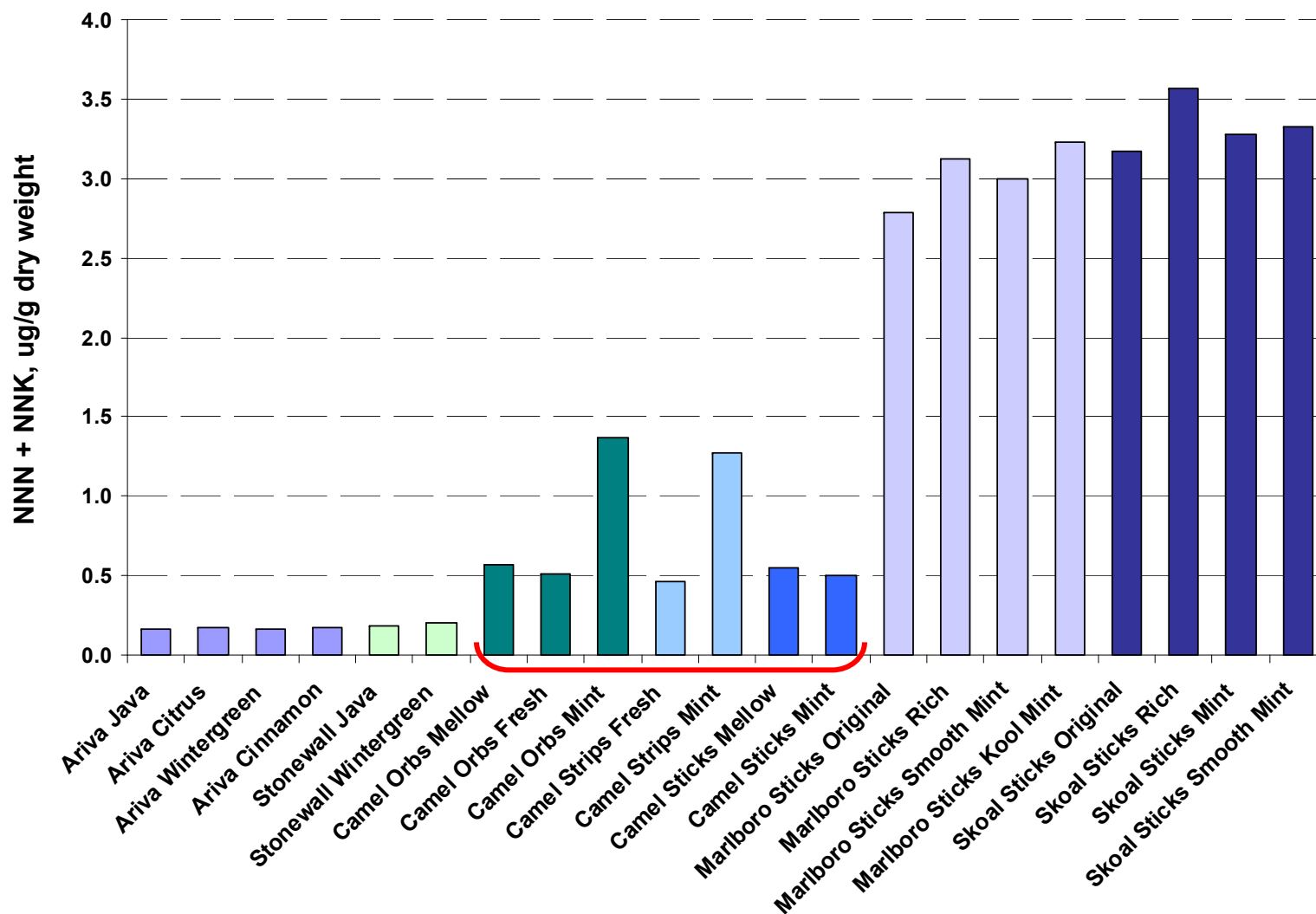
NNN










NNK

- In laboratory animals:
 - NNN causes esophageal cancer; NNK causes lung and pancreatic cancer; a mixture of NNN and NNK produces oral tumors
- In humans:
 - Exposure to NNN is associated with the risk of esophageal cancer, and exposure to NNK is associated with lung cancer in smokers
- Classified by IARC as carcinogenic to humans (Group 1)








Tobacco-specific *N*-nitrosamines (levels per gram dry weight)










Tobacco-specific *N*-nitrosamines in Camel dissolvable products

Product and flavor	Year of purchase	Version	Portion weight, g	% Moisture	µg/g dry weight		
					NNN	NNK	NNN+NNK
Orbs Mellow	2010		0.248	12.1	0.231	0.340	0.571
Orbs Fresh	2010		0.242	11.9	0.211	0.297	0.509
Orbs Mint	2011		0.234	7.8	0.297	1.08	1.37
Strips Fresh	2010		0.128	18.3	0.179	0.281	0.459
Strips Mint	2011		0.219	9.8	0.379	0.889	1.27
Sticks Mellow	2010		0.569	13.4	0.235	0.312	0.547
Sticks Mint	2011		0.462	6.4	0.260	0.239	0.499








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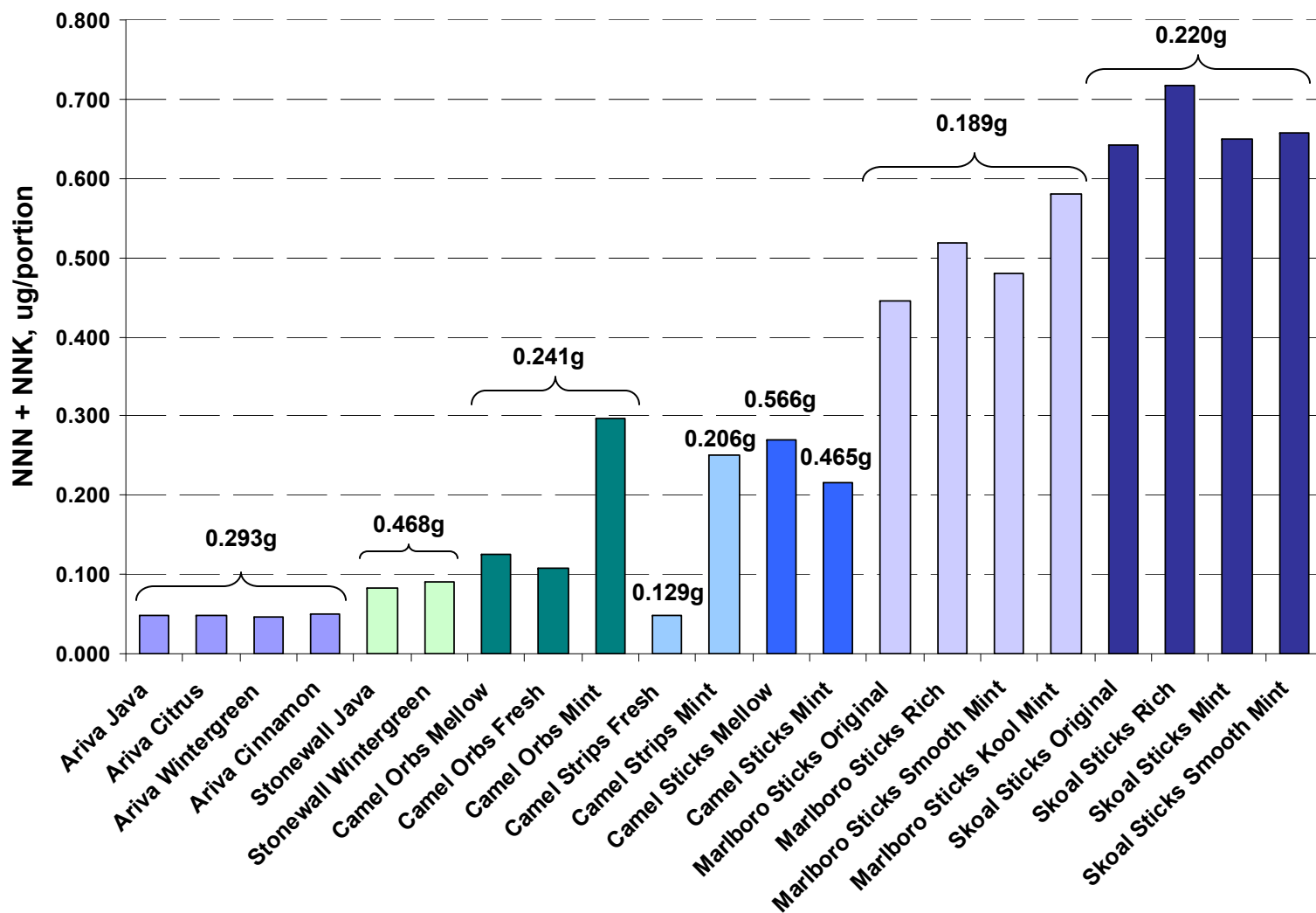
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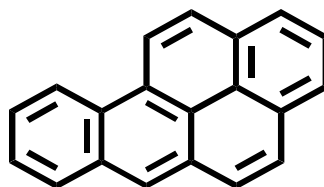
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Tobacco-specific *N*-nitrosamines (amounts in single portions)



Polycyclic Aromatic Hydrocarbons (PAH)



benzo[a]pyrene

- Formed during the incomplete combustion of organic matter
- Wide range of toxic effects in different organ systems
- Some are carcinogens
- Relatively high levels detected in U.S. moist snuff



Polycyclic aromatic hydrocarbons (levels per gram dry weight)

Product	ng/g dry weight		
	BaP	Carcinogenic (8)	Total (17)
Ariva	0.42	2.1	20.8
Stonewall	0.25	1.7	25.7
Camel Orbs	0.65	4.2	35.1
Camel Sticks	0.23	1.3	16.2
Camel Strips	1.2	5.7	76.6
Marlboro Sticks	1.0	4.1	78.7

^a BaP + benz[*a*]anthracene, chrysene, benzo[*b*]fluoranthene, benzo[*j*]fluoranthene, benzo[*k*]fluoranthene, indeno[1,2,3-*cd*]pyrene, and dibenz[*a,h*]anthracene

^b Carcinogenic (8) + acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, benzo[*e*]pyrene, benzo[*g,h,i*]perylene



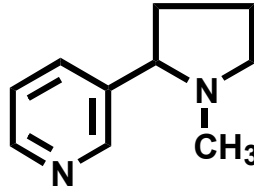
Polycyclic aromatic hydrocarbons (amounts in single portions)

Product	ng/g portion		
	BaP	Carcinogenic (8) ^a	Total (17) ^b
Ariva	0.12	0.59	5.9
Stonewall	0.11	0.79	11.6
Camel Orbs	0.14	0.91	7.6
Camel Sticks	0.11	0.58	7.6
Camel Strips	0.16	0.76	9.5
Marlboro Sticks	0.16	0.69	12.9

^a BaP + benz[*a*]anthracene, chrysene, benzo[*b*]fluoranthene, benzo[*j*]fluoranthene, benzo[*k*]fluoranthene, indeno[1,2,3-*cd*]pyrene, and dibenz[*a,h*]anthracene

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Nicotine



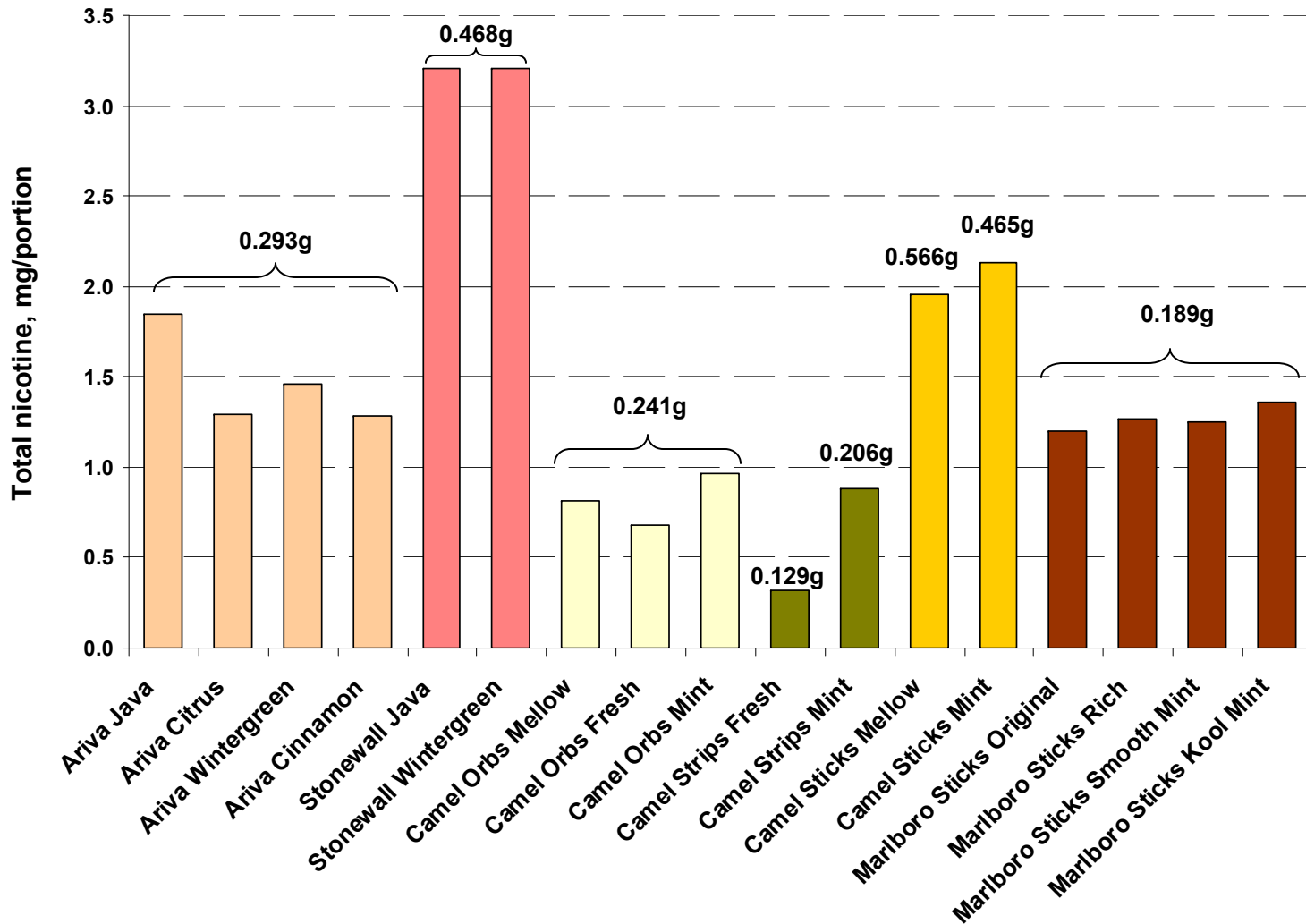
- The major known addictive constituent of tobacco
- Associated with fetal toxicity and cardiovascular risk factors
- Unprotonated nicotine easily crosses cellular membranes (biologically available form)
- The amount of nicotine present in unprotonated form depends on product pH



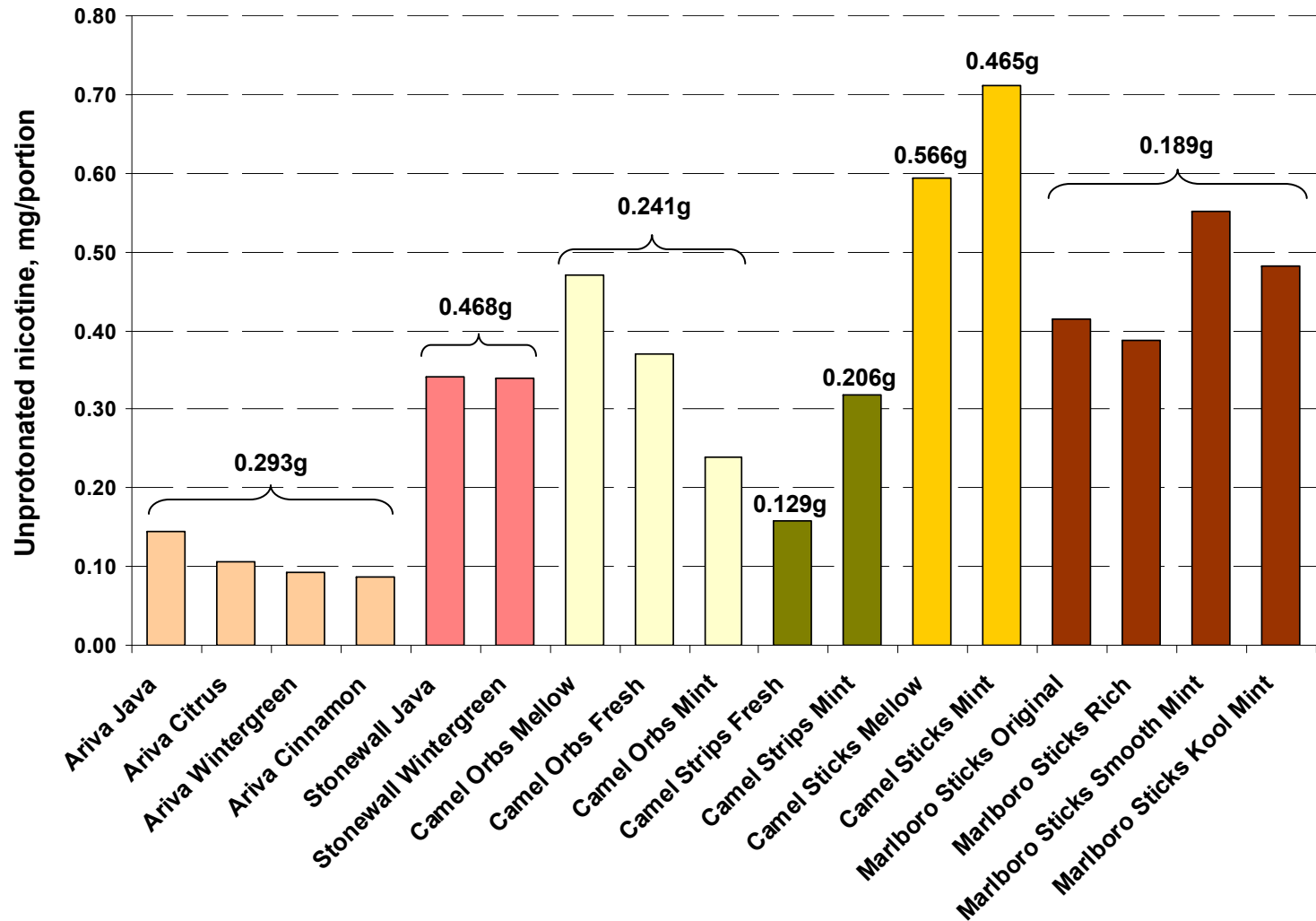
Nicotine (levels per gram dry weight)

Product and flavor	Total nicotine, mg/g	pH	Unprotonated nicotine	
			%	mg/g
Ariva Java	6.53	6.95	7.8	0.51
Ariva Citrus	4.56	6.97	8.2	0.37
Ariva Wintergreen	5.14	6.85	6.3	0.33
Ariva Cinnamon	4.38	6.89	6.8	0.30
Stonewall Java	7.17	7.10	10.6	0.76
Stonewall Wintergreen	7.06	7.10	10.6	0.75
Camel Orbs Mellow	3.72	8.16	58.0	2.16
Camel Orbs Fresh	3.19	8.10	54.6	1.74
Camel Orbs Mint	4.48	7.54	24.7	1.11
Camel Strips Fresh	3.05	8.01	49.4	1.51
Camel Strips Mint	4.48	7.77	36.0	1.61
Camel Sticks Mellow	3.97	7.66	30.4	1.21
Camel Sticks Mint	4.92	7.72	33.4	1.64
Marlboro Sticks Original	7.51	7.74	34.4	2.59
Marlboro Sticks Rich	7.63	7.67	30.6	2.34
Marlboro Sticks Smooth Mint	7.80	7.92	44.3	3.45
Marlboro Sticks Kool Mint	7.59	7.76	35.5	2.69

Total nicotine (amounts in single portions)



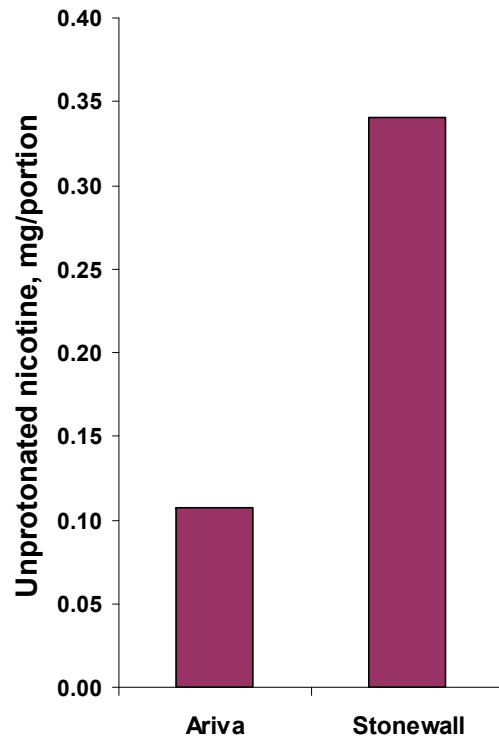
Unprotonated nicotine (amounts in single portions)



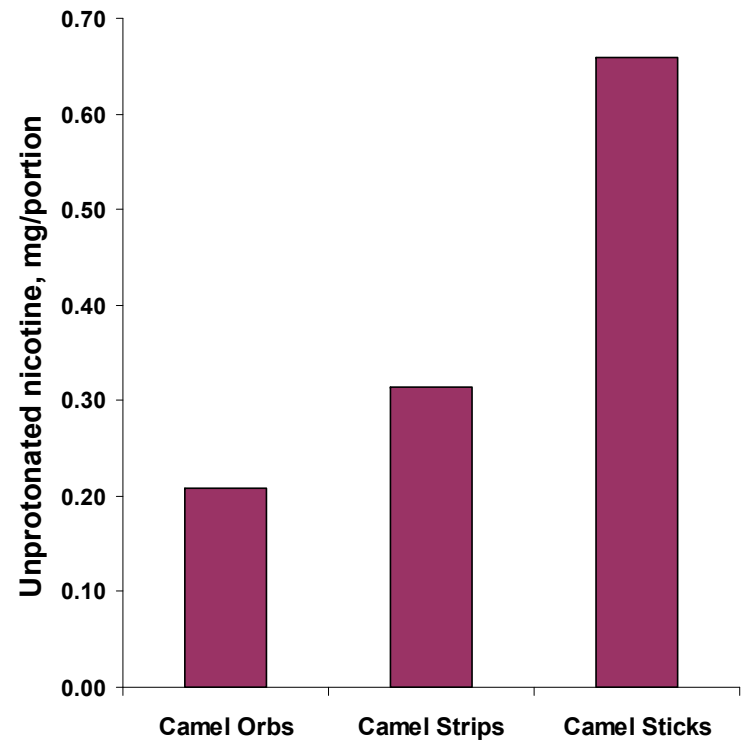


Unprotonated nicotine (amounts in single portions)

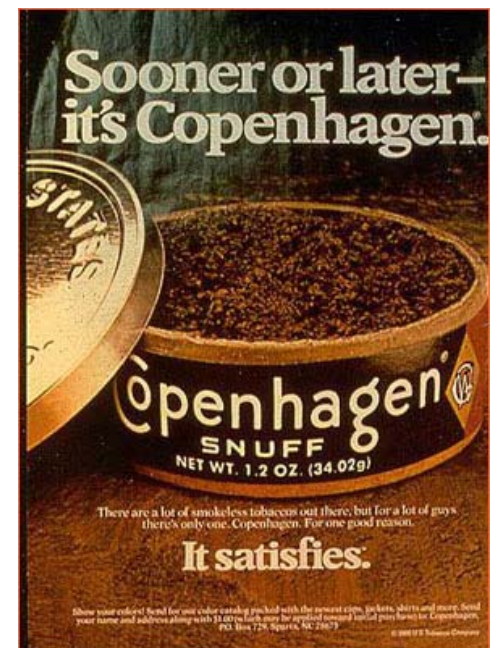
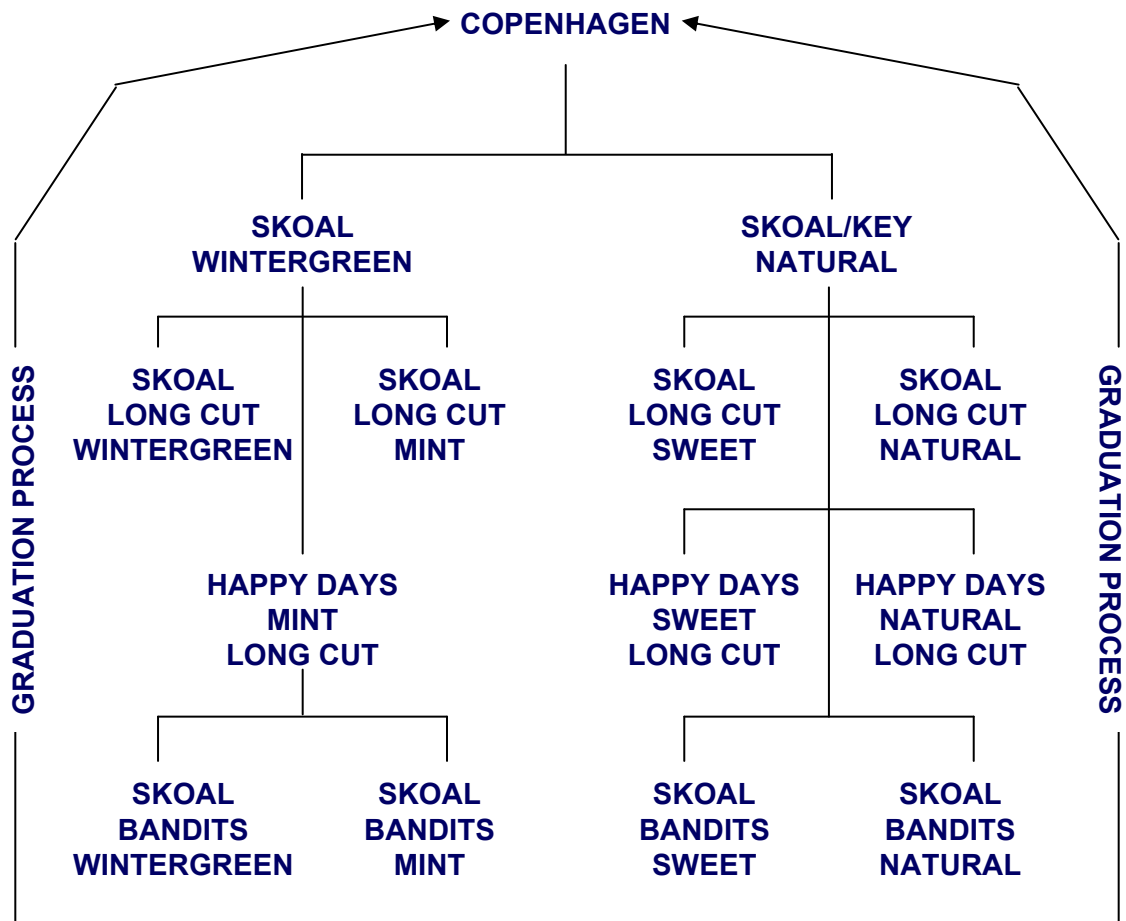
Star Scientific



RJ Reynolds



UST's "graduation strategy"





Summary:

Constituent levels

- **Wide range of nitrosamine levels among brands and products**
- **Variations in nitrosamine levels within the same product as it is being test-marketed and modified**
- **Relatively low levels of polycyclic aromatic hydrocarbons**
- **Larger variation in unprotonated nicotine levels than in total nicotine levels among products**



Summary:

Potential impact on public health

Toxicity and carcinogenicity

Adult users:
chronic exposures



From 0.05 to 0.7 ug NNN+NNK
per single dose

Children:
accidental poisoning



From ~1 to over 3 mg nicotine
per single dose

Addictiveness

Current smokers:
sustained tobacco use



An alternative in situations
where smoking is not allowed

New tobacco users:
addiction and graduation



Unprotonated nicotine levels
and gradient



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