

HPHC ANALYSIS OF WHITE FOX MODERN ORAL NICOTINE POUCH PRODUCTS

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ABSTRACT

FDA guidance is intended to assist in submitting premarket tobacco product applications (PMTAs) under section 910 of the FD&C Act which include reporting of HPHCs in tobacco and nicotine products and tobacco smoke under section 904(a)(3) of the FD&C Act.

The GN Tobacco White Fox Pouches are made by mixing synthetic nicotine with polacrilex and glycerol with inert substrates and adding flavors. The use of these products is similar to snus, the consumer places the product between the cheek and gum. The product belongs to the Category Other and subcategory Other. The FDA has not defined an appropriate list of HPHCs for products of this type. In the absence of guidance, GN Tobacco has chosen to follow the required list for portioned smokeless tobacco products. FDA recommends that companies analyze nine (9) chemicals.

The HPHC analysis was conducted on per pouch and estimated daily consumption basis. Among tested HPHCs, acetaldehyde, crotonaldehyde, cadmium, NNK or NNN levels were either not detected or below quantitative limits. Non-significant levels of formaldehyde and arsenic was found in White Fox products. The estimated daily use levels of formaldehyde and arsenic was compared with the oral no significant risk levels (NSRL) by OEHA-Cal-EPA and minimum risk level (MRL) by ASTDR. For all White Fox pouch products, the potential daily formaldehyde and arsenic exposure are significantly lower than the NSRL and MRL values thus presents minimal risk to the consumers.

STUDY DESIGN AND METHODS

The testing was conducted at Enthalpy Analytical LLC, Richmond, VA or Labstat International Inc., Kitchener, Ontario, Canada. Labstat facility has ISO/IEC 17025 accreditation with the American Association for Laboratory Accreditation (A2LA) as their accrediting body.

WHITE FOX NOVEL ORAL TOBACCO PRODUCTS

White Fox Product Description	Target Nicotine Level mg/pouch
White Fox Black Edition All White Slim Portion	20
White Fox Full Charge All White Regular Portion	18
White Fox All White Slim Portion	12
White Fox Double Mint All White Slim Portion	12
White Fox Peppered Mint All White Slim Portion	12

HPHC ANALYSES

Analysis Panel	Analytes	Replicates
Trace Metals	arsenic; cadmium	7
Nicotine	nicotine	7
Carbonyls	acetaldehyde; crotonaldehyde; formaldehyde	7
PAH	benzo(a)pyrene	7
TSNA	4-[methyl(nitroso)amino]-1-(3-pyridinyl)-1-butanone (NNK); N-nitrosornicotine (NNN)	7
pH	pH	7

METHOD SPECIFIC LOD AND LOQ FOR HPHC CONSTITUENTS

Analyte Name	Unit	LOD	LOQ
Acetaldehyde	µg/pouch	0.031	0.102
Crotonaldehyde	µg/pouch	0.036	0.120
Formaldehyde	µg/pouch	0.044	0.145
Arsenic	ng/pouch	3.51	11.7
Cadmium	ng/pouch	4.12	13.7
B(a)P, Benzo(a)pyrene	ng/pouch	0.033	0.111
NNK	ng/pouch	1.13	3.76
NNN	ng/pouch	0.739	2.46
Nicotine	µg/pouch	4.80	16.0

CONCLUSIONS

The HPHC analysis of the White Fox pouch products demonstrated the following:

- The carbonyl compounds (acetaldehyde and crotonaldehyde), metal (cadmium), nitrosamine compounds (NNK and NNN) and B(a)P were either not detected or below limits of quantitation.
- The non-significant and very low levels of formaldehyde and arsenic detected for the White Fox pouch products were below the CalEPA formaldehyde NSRL, ASTDR-Minimum Risk Levels (MRL) or the Derived No Effect Level (DNEL) for general population presenting minimal risk to the consumers.
- Compared to the FDA market authorized oral products, GN Tobacco White Fox pouch products have lower levels of HPHCs.
- Compared to a broad market sampling of modern oral nicotine products, GN Tobacco White Fox pouch products yield lower or similar levels of HPHCs.

RESULTS

HPHC ANALYSIS: PER POUCH BASIS

HPHC Constituents		White Fox All White Slim Portion		White Fox Double Mint All White Slim Portion		White Fox Full Charge All White Regular Portion		White Fox Black Edition All White Slim Portion		White Fox Peppermint All White Slim Portion	
	Unit	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Nicotine	mg/pouch	9.87	0.54	11.1	0.6	17.3	0.6	20.8	0.7	11.1	0.7
acetaldehyde	µg/pouch	BDL	NA	BDL	NA	NQ	NA	BDL	NA	NQ	NA
crotonaldehyde	µg/pouch	BDL	NA	BDL	NA	BDL	NA	BDL	NA	BDL	NA
formaldehyde	µg/pouch	2.46	0.82	2.65	0.69	3.99	0.50	2.89	0.63	3.30	0.42
arsenic	ng/pouch	15.5	1.2	13.7	1.2	13.8	3.1	14.6	1.4	14.3	1.4
cadmium	ng/pouch	BDL	NA	BDL	NA	BDL	NA	BDL	NA	BDL	NA
benzo(a)pyrene	ng/pouch	BDL	NA	BDL	NA	BDL	NA	BDL	NA	BDL	NA
pH	No unit	10.1	0.0	9.99	0.01	9.99	0.05	9.79	0.02	9.98	0.03
NNK	ng/pouch	BDL	NA	BDL	NA	BDL	NA	BDL	NA	BDL	NA
NNN	ng/pouch	BDL	NA	BDL	NA	BDL	NA	BDL	NA	BDL	NA

BDL: Below detection limit,
NQ: Not quantifiable,
NA: Not applicable

HPHC ANALYSIS: PRODUCT PER DAY USE BASIS

HPHC Constituents		White Fox All White Slim Portion	White Fox Double Mint All White Slim Portion	White Fox Full Charge All White Regular Portion	White Fox Black Edition All White Slim Portion	White Fox Peppered Mint All White Slim Portion
	Unit	Mean	Mean	Mean	Mean	Mean
acetaldehyde	µg/day	BDL	BDL	BDL	BDL	BDL
crotonaldehyde	µg/day	BDL	BDL	BDL	BDL	BDL
formaldehyde	µg/day	21.16	22.79	34.31	24.85	28.38
arsenic	ng/day	133.3	117.82	118.68	125.56	122.98
cadmium	ng/day	BDL	BDL	BDL	BDL	BDL
benzo(a)pyrene	ng/day	BDL	BDL	BDL	BDL	BDL
NNK	ng/day	BDL	BDL	BDL	BDL	BDL
NNN	ng/day	BDL	BDL	BDL	BDL	BDL

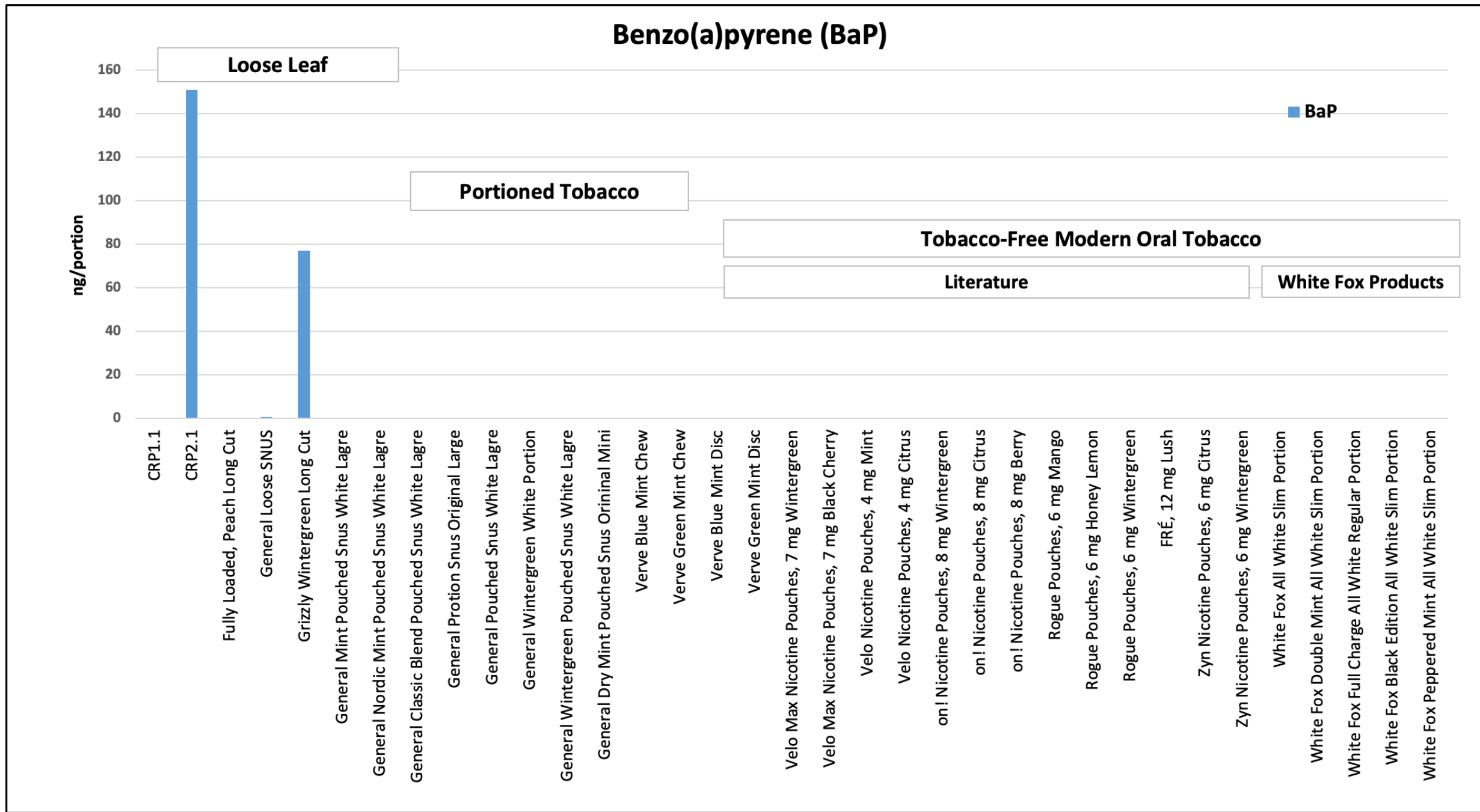
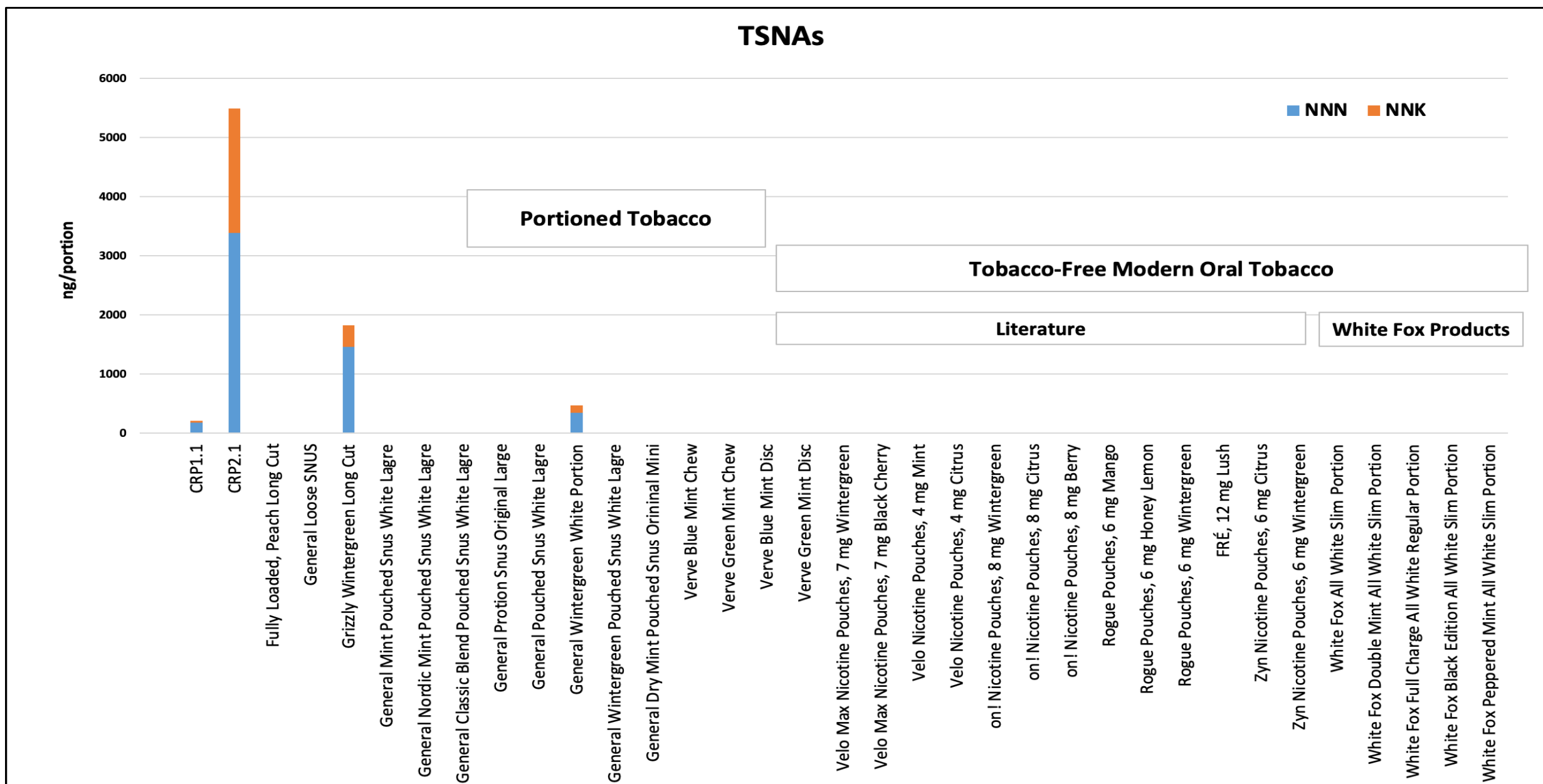
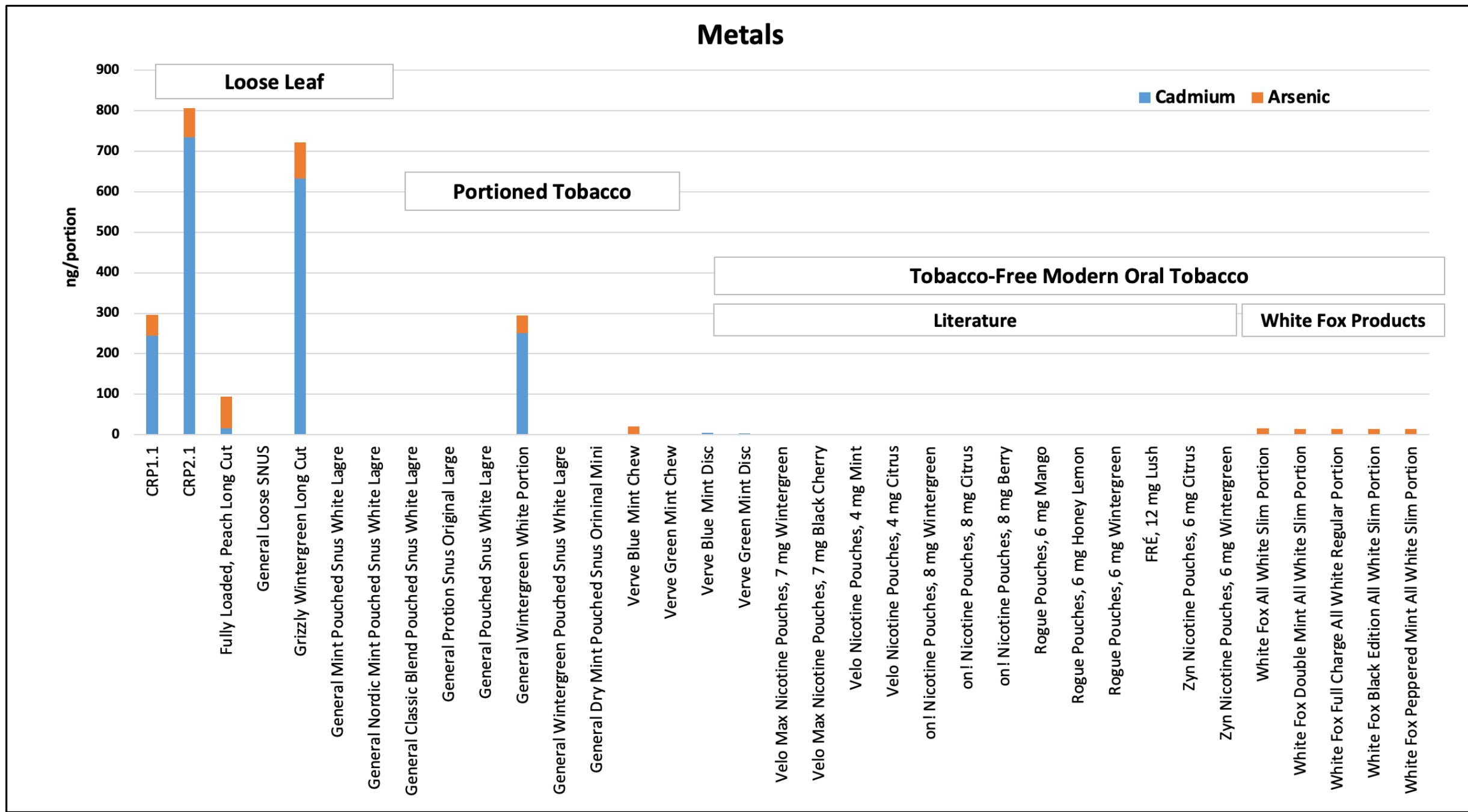
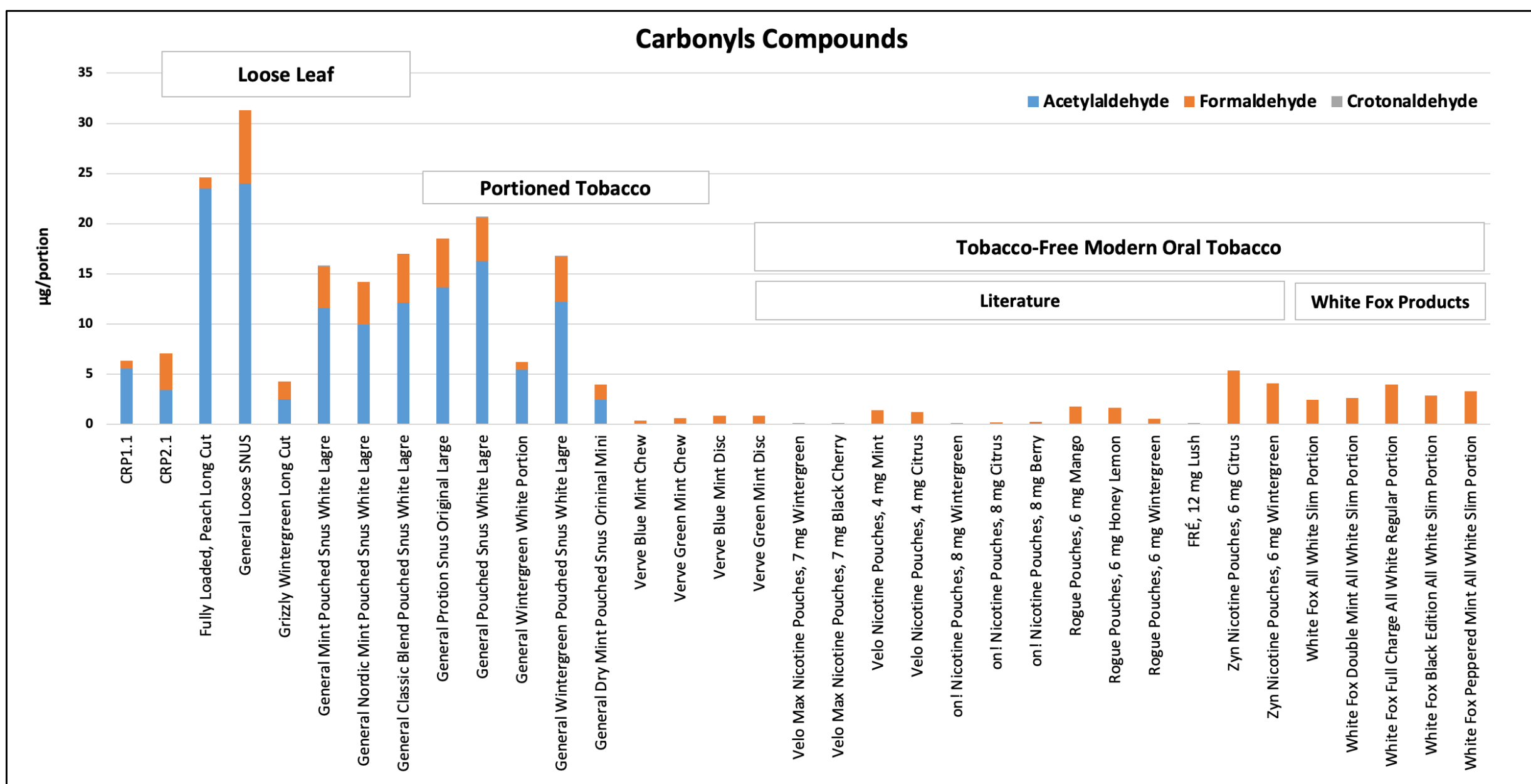
BDL: Below detection limit.
The calculated daily exposure based on 8.6 nicotine pouch/day consumption, Azzopardi et al. (2022)

COMPARATIVE
CALCULATED
EXPOSURE OF
FORMALDEHYDE
AND ARSENIC
FROM THE WHITE
FOX PRODUCTS TO
EXPOSURE LIMITS

Test Product / Exposure Limit Values	Unit	Formaldehyde				Unit	Arsenic			
		Calculated Daily Exposure	Fold Below Exposure Limits				Calculated Daily Exposure	Fold Below Exposure Limits		
			CalEPA-NSRL	ASTDR - MRL	ECHA-DNEL			CalEPA-NSRL	ASTDR - MRL	ECHA-DNEL
White Fox All White Slim Portion	µg/day	21.16	1.9	662	14	ng/day	133.3	75	158	893
White Fox Double Mint All White Slim Portion	µg/day	22.79	1.8	614	13	ng/day	117.82	85	178	1010
White Fox Full Charge All White Regular Portion	µg/day	34.31	1.2	408	8	ng/day	118.68	84	177	1003
White Fox Black Edition All White Slim Portion	µg/day	24.85	1.6	563	12	ng/day	125.56	80	167	948
White Fox Peppered Mint All White Slim Portion	µg/day	28.38	1.4	493	10	ng/day	122.98	81	171	968
CalEPA-NSRL	µg/day	40	NA	NA	NA	ng/day	10,000	NA	NA	NA
ASTDR - MRL	µg/day	14,000	NA	NA	NA	ng/day	21,000	NA	NA	NA
ECHA-DNEL (general population)	µg/day	287	NA	NA	NA	ng/day	119,000	NA	NA	NA

NA: Not applicable

COMPARATIVE HPHC LEVELS OF WHITE FOX POUCH PRODUCTS WITH MARKET COMPARATORS



REFERENCES

- ASTDR - MRL: Agency for Toxic Substances and Disease Registry MINIMAL RISK LEVELS (MRLs). (<https://www.cdc.gov/tsp/MRLS/mrlslisting.aspx>)
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- ECHA-DNEL: European Chemical Agency. Information on Chemicals (ECHA). <https://www.echa.europa.eu/information-on-chemicals>.
- FDA 2014. Estimated HPHC Intakes from Snus Consumption – Comparison with Dietary Intakes or Smoking. (https://www.accessdata.fda.gov/Static/widgets/tobacco/MRTP/20%20appendix-6c-environ%20hphc%20report%2020214_Redacted.pdf)
- Jablonski, J.J. et al. (2022) Market Survey of Modern Oral Nicotine Products: Determination of Select HPHCs and Comparison to Traditional Smokeless Tobacco Products. Separations, 9, 65.