# HPHC Analysis of Seven Flavors of a Temperature-Regulated Nicotine Salt Pod System

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## Introduction

Combustible cigarettes reach temperatures in excess of 900 degrees Celsius[1] and consequently generate over seven thousand[1] thermal degradation products including compounds characterized as Harmful and Potentially Harmful Constituents (HPHCs) under the Food, Drug and Cosmetic Act (FD&C Act)[2]. The JUUL system is a temperature-regulated closed nicotine salt pod system (NSPS) possessing no user modifiable settings with the design intent of minimizing combustion byproducts across a range of operating environments. The NSPS pods evaluated in these studies utilized a cotton wicking material to supply e-liquid for aerosolization. Seven different flavors, each at a nicotine concentration of 18 mg/mL, were analyzed for a select panel of analytes and HPHCs listed in the US FDA PMTA draft guidance document[2] for Electronic Nicotine Delivery Systems (ENDS) in comparison to a 3R4F Kentucky Reference Cigarette. The NSPS Pods contain 5 major ingredients: nicotine, benzoic acid, glycerol, propylene glycol, and flavorants. At present, formulations in 18 mg/mL nicotine concentration are available in ex-US markets.

## Materials and Methods

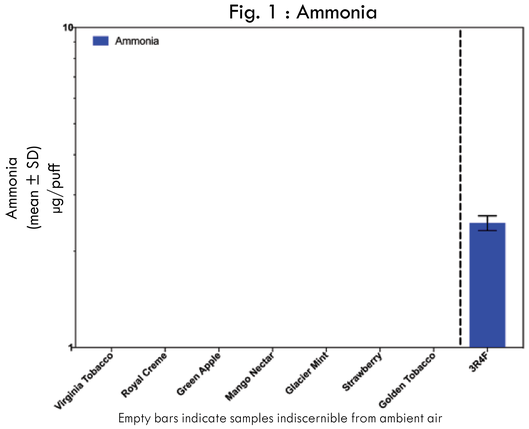
The aerosol HPHC profile generated by actuating NSPS pods with cotton wicking were evaluated by an accredited ISO 17025 3rd party laboratory (Labstat International) using validated analytical methods. E-liquid flavors loaded into the tested pods spanned a combination of tobacco, mint/menthol, and fruit flavors (including Royal Creme, Green Apple, Mango Nectar, Glacier Mint, Strawberry, Golden Tobacco, Virginia Tobacco), all at nicotine concentrations of 18 mg/mL. Vaping topography was set at a 70 ml square wave volume puffed across a 3 second duration with a 30 second puff interval. Each analytical replicate was generated using a unique pod with 10 replicates collected for each assay. 3R4F Kentucky Reference Cigarette replicates were smoked on a smoking machine under the Health Canada defined "intense puffing regime". A panel of 22 analytes was tested covering six categories of HPHCs - polyaromatic hydrocarbons (PAH), carbonyls, metals, tobacco specific nitrosamines (TSNAs), polyaromatic amines (PAA), and volatile organic compounds (VOC). Quantifiable means and standard deviations (±SD) for each analyte are represented visually by bars. Sample values below the limit of quantitation (LOQ) are visually represented by dashed bars set to the magnitude of the method LOQ divided by √2. Sample values that were indiscernible from ambient air controls are not visually represented.



## Results

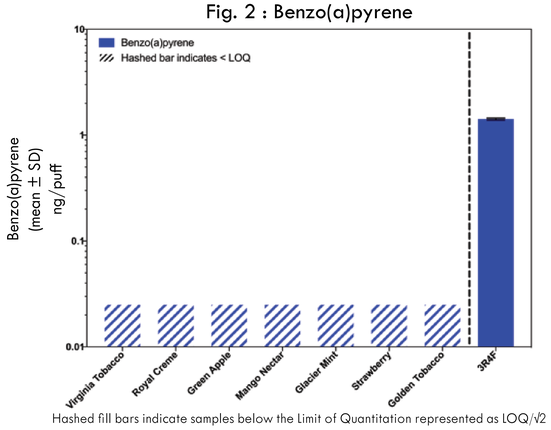
HPHCs expected as constituents in the NSPS aerosol such as nicotine, propylene glycol, and glycerol were identified analytically but excluded from subsequent representation. All formulations tested across the 22 panel analytes measured in these categories were evaluated against the Kentucky 3R4F reference combustible cigarette in order to generate a comparison of relative exposure. 95% of NSPS aerosol analytes were below the level of quantification. Notably, VOCs (acrylonitrile, benzene, 1,3-butadiene, isoprene, and toluene) and select carbonyls (diacetyl, acetyl propionyl, and crotonaldehyde) were uniformly below the level of detection in the aerosol generated by all seven flavors under these puffing machine conditions. NSPS aerosol composition for all seven flavors was also found to be markedly different from the mainstream smoke of the 3R4F reference combustible cigarettes, eliciting a 99% reduction in assessed HPHCs.

Fig. 1 : Ammonia



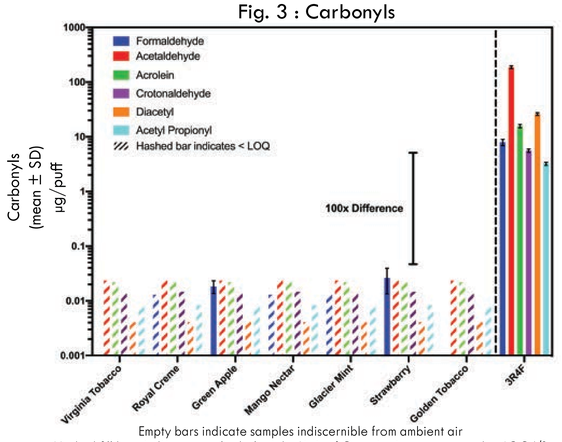

Empty bars indicate samples indiscernible from ambient air

Fig. 2 : Benzo(a)pyrene



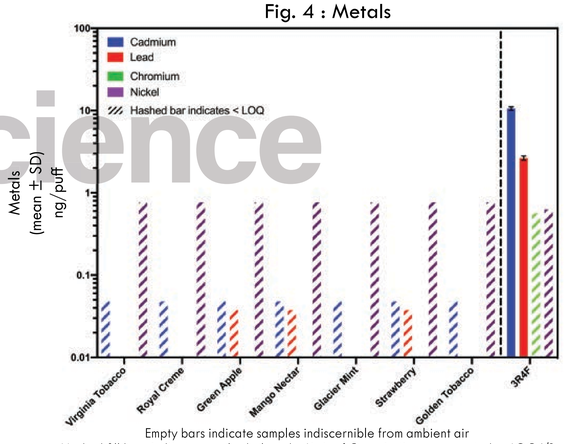

Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2

Fig. 3 : Carbonyls



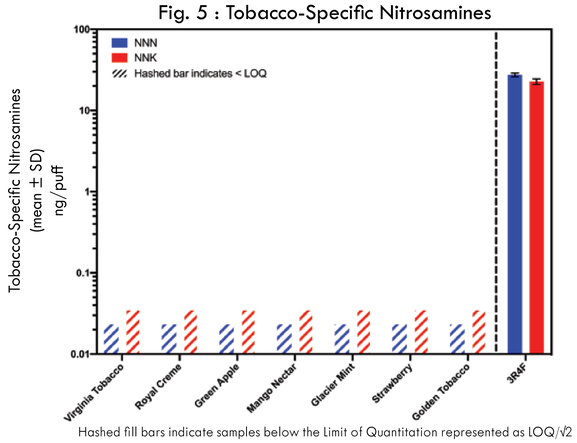

Empty bars indicate samples indiscernible from ambient air
Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2

Fig. 4 : Metals



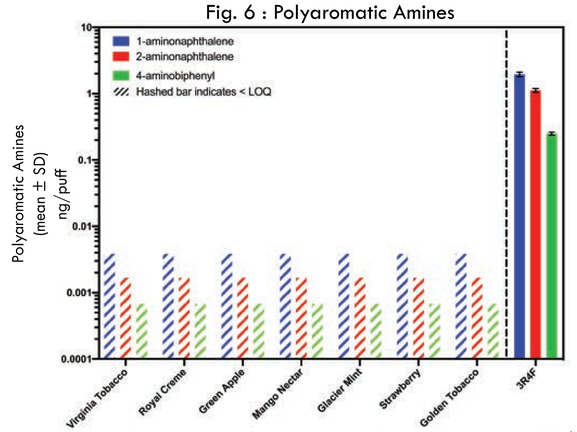

Empty bars indicate samples indiscernible from ambient air
Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2

Fig. 5 : Tobacco-Specific Nitrosamines



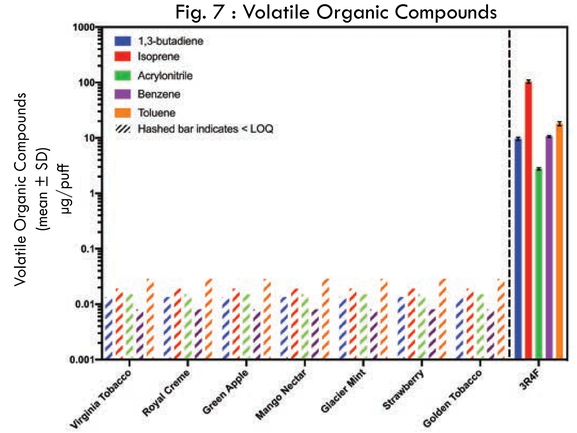

Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2

Fig. 6 : Polyaromatic Amines




Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2

Fig. 7 : Volatile Organic Compounds




Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2

## Conclusion

Consistent with prior research, NSPS pods using a cotton wicking material demonstrated average reductions of > 99% in a standardized list of HPHCs compared to reference combustible cigarettes.

## Limitations

This was a preliminary assessment of ten replicates of each analytical method for each formulation, using one puffing regime on a puffing machine under laboratory conditions. Comprehensive characterization of human HPHC exposure requires user topography data and biomarker analyses.

## References

1. U.S. Department of Health and Human Services, "Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General", 2012.
2. FDA Draft Guidance, "Premarket Tobacco Applications for ENDS Products", May 2016.
3. G. Gilman, M. Johnson, A. Martin, M. Misra, "HPHC Analysis of Eight Flavors of a Temperature-Regulated Nicotine Salt-Based ENDS Product", Dec 2018.



**Note: Consistent with applicable laws and regulations, JUUL Labs does not, and cannot, promote its products as being less harmful than cigarettes.**