

# Experimental Design and Results from Non-Targeted Analyses of glo Heated Tobacco Products



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# Agenda

- 1** Study Objective
- 2** Analytical Characterization of glo HTP Aerosols
- 3** Toxicological Evaluation of Compounds Found in glo HTP Aerosols
- 4** Conclusions
- 5** Acknowledgements & Questions

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# Study Objective

## *Why perform non-targeted analyses?*

### FDA's 2021 PMTA final rule

Requires “a **full statement of the constituents**, including **HPHCs** [harmful and potentially harmful constituents] and **other constituents**, contained within, or emitted from (including its smoke or **aerosol**)” a **new tobacco product**.

### Regulatory Research Priorities

One of the stated **research focuses** for the **FDA Center for Tobacco Products** includes “**understanding the chemical constituents in tobacco products** and the methods for measuring them **across products with diverse chemical characteristics**.”

### Foundational to THR Science

The **comprehensive chemical characterization** of glo HTP aerosol lays the foundation of a larger **tobacco harm reduction (THR)** platform, built upon by further scientific evaluations.

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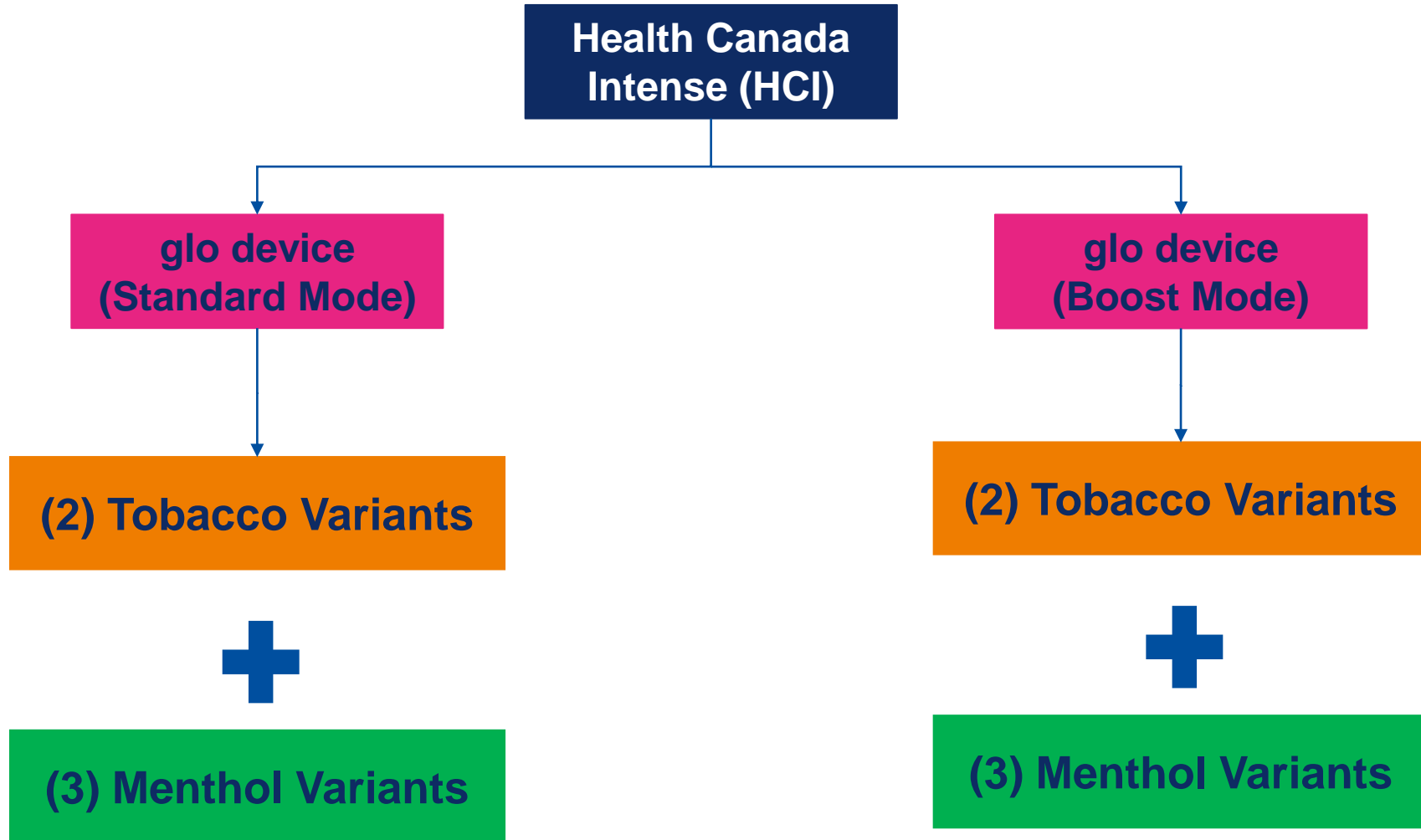
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## What is glo?



1. Heated Tobacco Product
2. Consumable comes in the following formats:
  - A. (2) Tobacco Variants
  - B. (3) Menthol Variants
3. The device heats the consumables using two thermal profiles
  1. Standard Mode (heats to 250°C for 4 minutes)
  2. Boost Mode (heats to 260°C for 3 minutes)
4. Aerosol is created below pyrolysis and combustion ranges.

# Test Products





# Sample Collection and Analysis

## Analysis 1:

**Particulate Phase**  
Analyzed by  
LC/MS/MS  
Positive Polarity

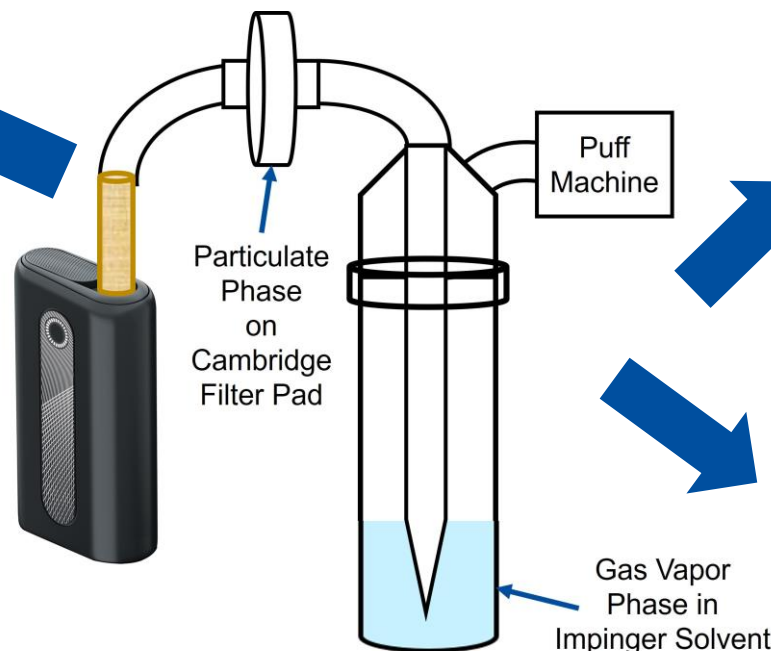


## Analysis 2:

**Particulate Phase**  
Analyzed by  
LC/MS/MS  
Negative Polarity



Non-volatile and  
semi-volatile



Internal Reference Library +  
NIST 20 Database

## Analysis 3:

**Particulate Phase + Gas  
Vapor Phase = Total  
Aerosol**  
Analyzed by Direct  
Injection GC/MS



## Analysis 4:

**Gas Vapor Phase**  
Analyzed by  
Headspace GC/MS



Volatile and  
semi-volatile

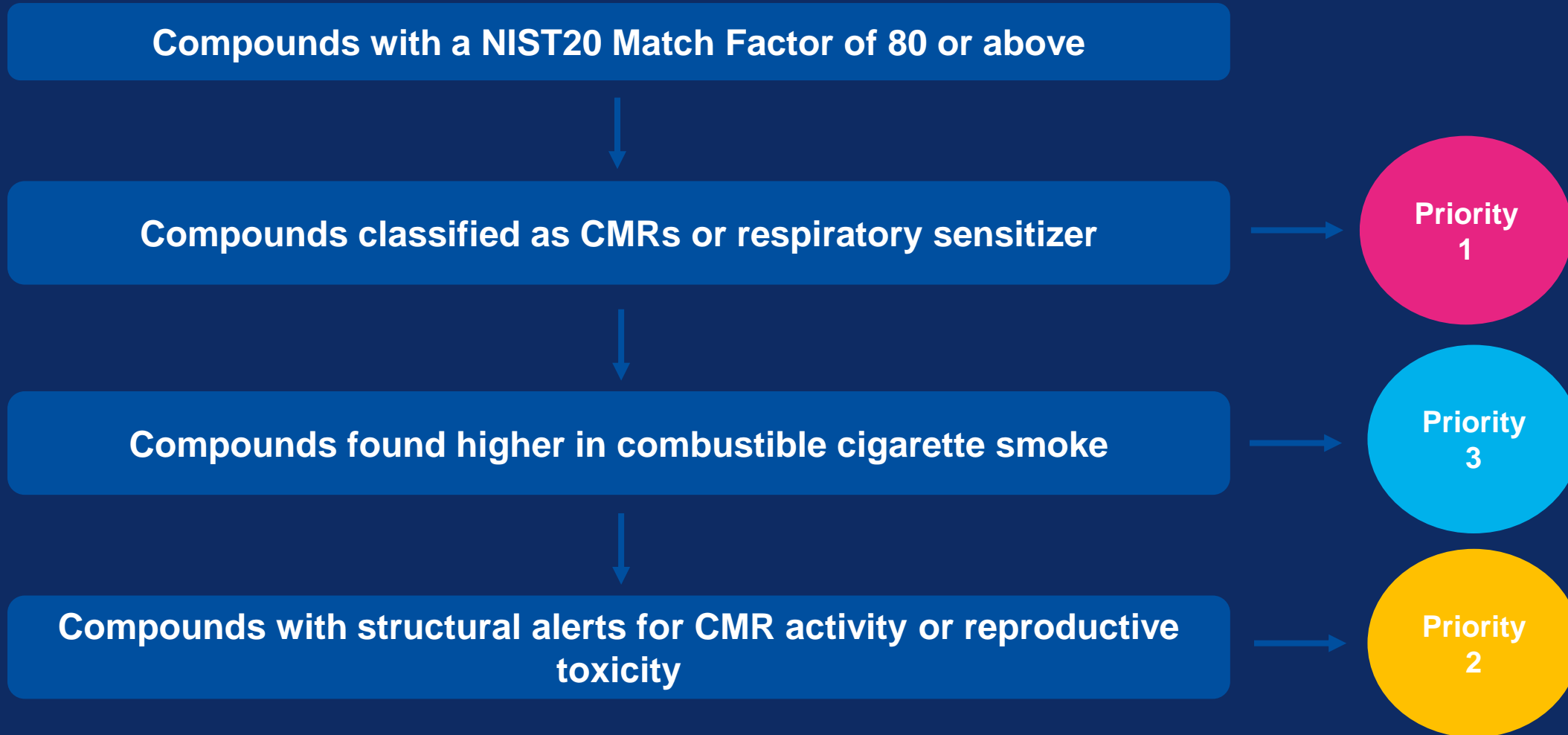
## 2 Data Processing

1. Semi-quantitation occurred with internal standards to estimate concentration of compounds.
2. Analytical Thresholds (AT), based on lower working ranges for each method, were applied to peak replicates that had a semi-quant value below the AT.
3. Compounds found in the solvent blanks were subtracted from the sample signals.
4. Descriptive data, such as SMILES data, were added to each compound and obsolete CAS # were corrected prior to routing for tox evaluation.

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### 3 Toxicological Prioritization Process



CMR = carcinogen, mutagen, developmental and/or reproductive toxicants

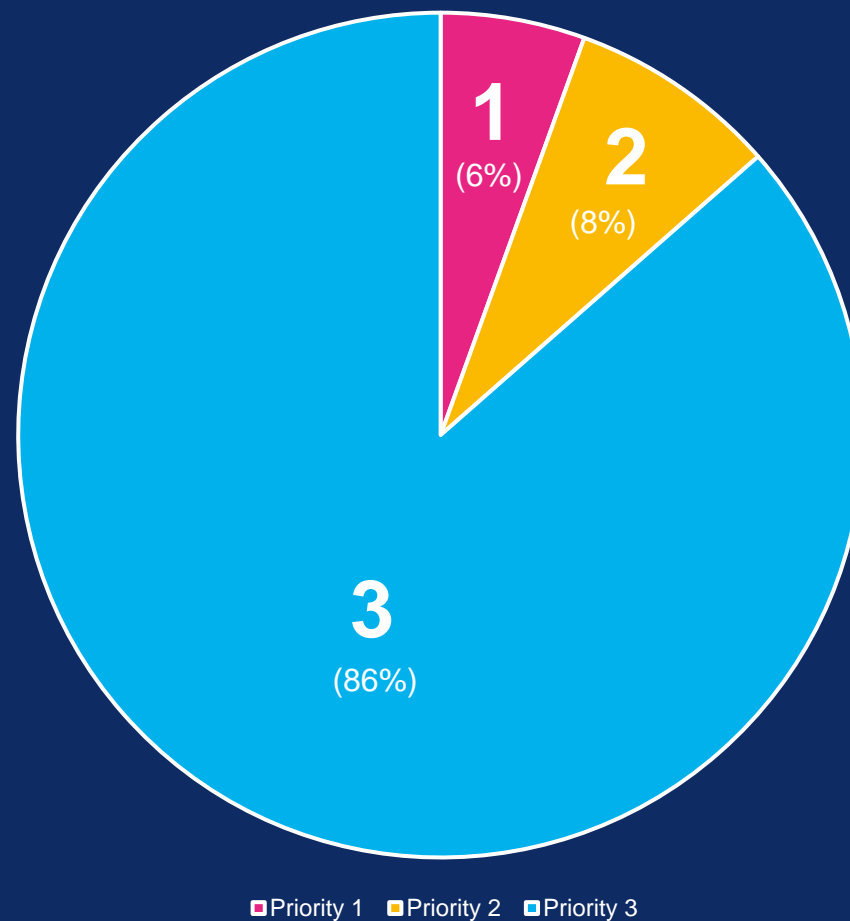
# Results of Prioritization Scheme

Total Semi-Quant  
Compounds

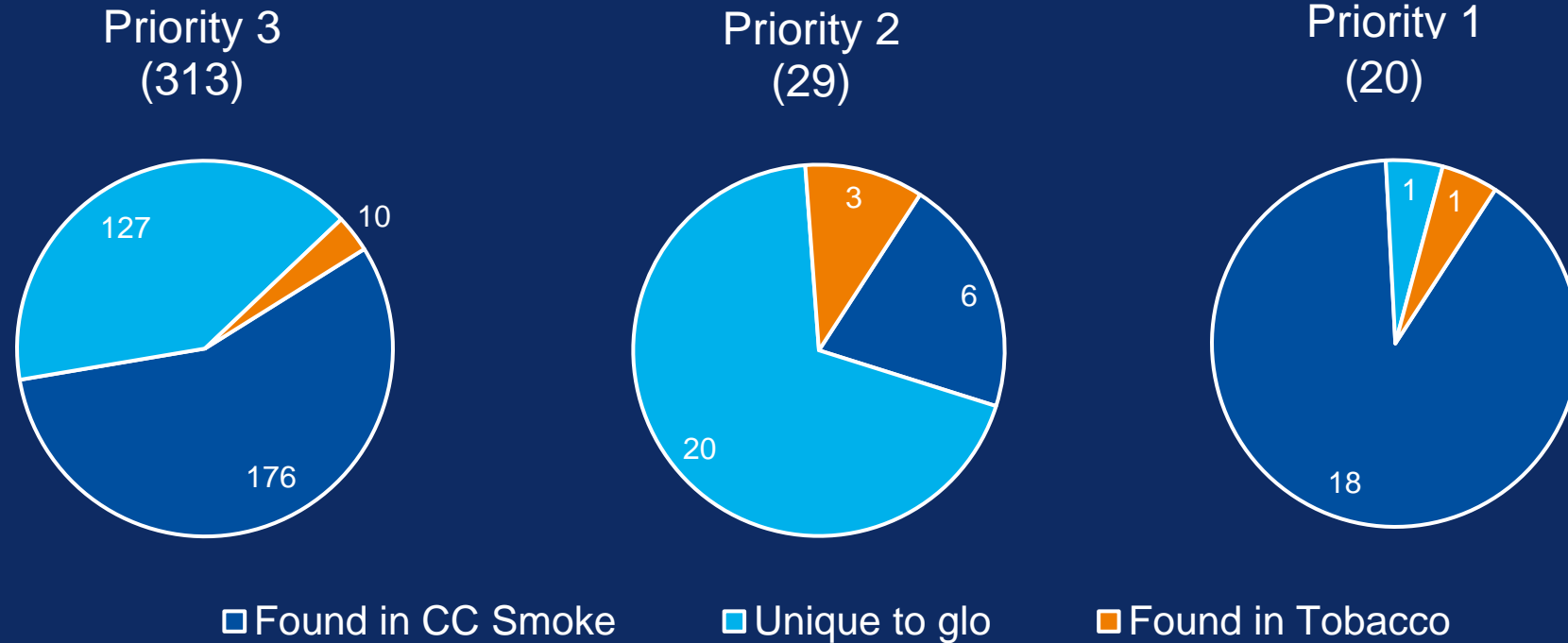
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362

High Confidence  
IDs for Tox  
Assessment



# Results of Prioritization Scheme



### 3

# Priority 1 Compounds

19 of 20 Priority 1 Compounds are known constituents of combustible cigarette smoke or tobacco

Compound	Classification	Literature Reporting	Percent Reduction* (glo from 3R4F)	
1	Carcinogen	Quantified in Combustible Cigarette Smoke	97 - 99	
2	Carcinogen		93 - > 99	
3	Mutagen		97 - 98	
4	Mutagen, Carcinogen		65 - 91	
5	Carcinogen		86 - 94	
6	Mutagen, Carcinogen		93 - 95	
7	Mutagen, Carcinogen		> 99	
8	Mutagen, Carcinogen		89 - 96	
9	Respiratory Sensitizer, Developmental Toxicant		97	
10	Mutagen, Carcinogen		94	
11	Mutagen		72	
12	Mutagen, Carcinogen, Reproductive Toxicant		81 - 87	
13	Mutagen, Carcinogen		-13 - 68	
14	Respiratory Sensitizer ***	Present in Combustible Cigarette Smoke		
15	Developmental Toxicant			
16	Developmental Toxicant, Carcinogen			
17	Reproductive and Developmental Toxicant ***			
18	Reproductive Toxicant, Carcinogen			
19	Carcinogen		Present in Tobacco	
20	Mutagen, Carcinogen ** / ***		Unique to glo	

\*Calculated using the maximum yields across all neo stick variants and device modes tested

\*\*Classified by its parent compound

\*\*\*Only found in 1 out of 10 samples (variants and modes)

### 3 Supporting Data

- Targeted analyses of HPHCs (harmful and potentially harmful constituents)
- *in vitro* testing
  - Ames Mutagenicity
  - *in vitro* Micronucleus – chromosome damage
  - Neutral Red Uptake – cytotoxicity
  - EpiAirway MTT cytotoxicity
  - EpiAirway oxidative stress
  - Cell Transformation Assay – tumor promotion potential

**glo HTP aerosols have lower levels of most constituents than combustible cigarette smoke**

**glo HTP aerosol is far less toxic *in vitro* than combustible cigarette smoke**



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**Overall, glo HTP aerosols contain fewer and significantly lower levels of constituents than combustible cigarette smoke**

- 708 compounds were identified in the aerosol of glo HTP across all neo stick variants
  - ~250 compounds per variant
  - Combustible cigarette smoke is known to contain more than 7000 compounds
- Toxicological reviews determined that the overall toxicological impact of glo HTP aerosol exposure on the consumer is likely to be less than that of combustible cigarette smoke, consistent with supporting *in vitro* data
- Study results are consistent with the abundance of chemistry, non-clinical toxicology, and clinical data submitted to FDA, supporting a conclusion that the use of glo HTPs is likely to present substantially less harm to individuals than cigarette smoking

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