

Comparative Quantitative Health Risk Assessment (QRA) Of A Temperature-Regulated Nicotine Salt-Based Connected ENDS Product with Tobacco Cigarette: Aerosol Cancer and Non-Cancer Risks

Manoj Misra, Ed Carmines, Lise Fraissinet

Chemular Inc, Hudson MI, USA

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ABSTRACT

The Glas G² ENDS is a temperature-regulated nicotine salt pre-filled disposable pod connected system (Glas system). This work adopted the QRA approach to evaluate and present a comparison of reduced exposure (selective HPHCs) and corresponding potential cancer and non-cancer risks for the Glas G² system with tobacco, menthol and non-tobacco-non-menthol formulations in comparison to the tobacco combustible reference cigarette, 3R4F and Market cigarettes, machine vaped/smoked under non-intense and intense puffing conditions.

Exposure concentrations (EC) were estimated assuming a lifetime continuous exposure using the equations.

Tobacco cigarette: $AC \times CPD \times ED \times EF / DIR \times AT$
Glas ENDS: $AC \times (PC \times PV) \times ED \times EF / DIR \times AT$

where EC, exposure concentration; AC, analyte concentrations under non-intense and intense conditions; CPD, cigarettes per day (20 for tobacco cigarettes); E, exposure duration (64.4 years); EF, exposure frequency (365 days); DIR, daily inhalation rate (20 m3/day); AT, averaging time (25550 days); PC, puff count (worst-case 400 puffs), and PV, puff volume (Glas: 0.055 Liter for non-intense and 0.11 Liter for intense and Tobacco cigarettes: 0.035 Liter ISO non-intense and 0.055 Liter Health Canada intense).

Non-cancer risks were quantified using the hazard quotient (HQ) approach and cancer risks were estimated by calculating the incremental lifetime cancer risk (ILCR), utilizing non-cancer and cancer toxicity values issued by government agencies or published in peer-reviewed literature. Data revealed that, the modelling of exposure to HPHCs in Glas ENDS products aerosols lead to a marked reduction when compared to the smoke from tobacco combustible cigarette under both non-intense and intense vaping conditions, indicating the potential for significant reduced (>99%) non-cancer and cancer health hazard risks.

STUDY OVERVIEW

AEROSOL CHEMISTRY

Selected US FDA abbreviated Harmful and Potentially Harmful Constituent (HPHC) constituents were the focus of this assessment (acetaldehyde, acrylonitrile, acrolein, benzene, crotonaldehyde, formaldehyde and toluene) since cancer and non-cancer toxicity values are available for risk assessment.

The levels of these selected HPHCs in the Glas ENDS products, Kentucky reference cigarette (3R4F) and market tobacco cigarette are listed in Table 1. For all Glas product aerosol HPHC analytes, all values below LOD replaced by value of LOD/2 for risk assessment.

The Products, Vaping/Smoking Profiles and HPHC Data Source

	Vaping/Smoking Profile		HPHC Data Source
	Non-intense	Intense	
Glas: Blonde Tobacco 50 mg/mL	CORESTA CRM81	110 mL puff volume, 5 sec puff duration, 30 sec puff interval	Glas, PMTA Submission
Glas: Fresh Menthol 50 mg/mL			
Glas: Gold 50 mg/mL			
3R4F Kentucky Ref. Cigarette			
VLN Regular King	ISO	HCI	Jaccard et al. 2019
VLN Menthol King			
Marlboro Gold King Box			
Marlboro Menthol Gold King Soft Pack			
Marlboro Red King Soft Pack			
Camel Blue King			
Newport Menthol Green King	ISO	HCI	HPHC information provided to the FDA pursuant to Section 904(a)(3) of the Federal Food, Drug, and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act.

EXPOSURE CONCENTRATIONS (EC)

The exposure parameters and assumptions to calculate the Lifetime Average Daily Intake (LADI) for combustible tobacco cigarette

Exposure Parameters	Symbol	Value	Unit	Source
Cigarettes consumption	CpD	20	cigarettes/day	USFDA (2013)
Exposure frequency	EF	365	days/year	Maximum value
Exposure duration, cigarettes	ED	64.4	years	USFDA (2013)
Inhalation rate	DIR	20	m³/day	USEPA (2011)
Averaging time	AT	25,550	days	USEPA (2014)

The exposure parameters and assumptions to calculate the Lifetime Average Daily Intake (LADI) for Glas products

Exposure Parameters	Symbol	Value	Unit	Source
Puff count	PC	163	Puff/day	Dautzenberg and Damien Bricard (2015)
Puff Volume (non-intense)	PV	0.055	Liter	
Puff Volume (intense)	PV	0.110	Liter	
Exposure frequency	EF	365	days/year	Maximum value
Exposure duration, cigarettes	ED	64.4	years	USFDA (2013)†
Daily Inhalation rate	DIR	20	m³/day	USEPA (2011)
Averaging time	AT	25,550	days	USEPA (2014)

Lifetime Average Daily Intake (LADI, µg/m³) calculations

COMBUSTIBLE CIGARETTE	GLAS PRODUCTS	Non-Cancer Risk	Cancer Risk
LADI = AC x CpD x ED x EF / DIR x AT	LADI = AC x (PC x PV) x ED x EF / DIR x AT	HQ = LADI ÷ RfC Cumulative HQ = Σi HQ	ILCR = LADI x IUR Cumulative ILCR = Σi ILCRi
		HQ - Hazard Quotient RfC - Reference Concentration	ILCR - Incremental Lifetime Cancer Risk IUR - Inhalation Unit Rate

TOXICITY VALUES CONSIDERED FOR RISK ASSESSMENT

Constituent	CANCER		NON-CANCER	
	IUR (µg/m³)	Source	RfC (mg/m³)	Source
Acetaldehyde	2.20E-06	IRIS, 1988	0.00900	USEPA, 1991
Acrolein	N/A	N/A	0.00002	USEPA, 2003
Acrylonitrile	6.80E-05	IRIS 2018	0.00200	USEPA, 1991
Benzene	7.80E-06	IRIS 2000	0.03000	USEPA, 2003
Crotonaldehyde	3.27E-05	TECQ, 2015	0.01000	TECQ, 2015
Formaldehyde	1.30E-05	IRIS, 1988	0.01000	ATSDR, 1999
Toluene	N/A	N/A	5.00000	USEPA, 2005

RESULTS

QUANTITATIVE NON-CANCER RISK ASSESSMENT OF GLAS ENDS PRODUCTS EMISSION CONSTITUENTS COMPARED TO COMBUSTED CIGARETTE

	GLAS PRODUCTS						KENTUCKY REF.CIGARETTE		NON-CANCER RISK (HQ)										MARKET CIGARETTE			
	Blonde Tobacco (50 mg/mL)		Fresh Menthol (50 mg/mL)		Gold (50 mg/mL)		3R4F		VLN Regular King		VLN Menthol King		Marlboro Gold King Box		Marlboro Menthol Gold King Soft Pack		Marlboro Red King Soft Pack		Camel Blue King		Newport Menthol Green King	
	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense
Acetaldehyde	1.31E-04	1.02E-03	1.53E-04	1.28E-03	1.31E-04	1.02E-03	6.10E+01	1.88E+02	6.61E+01	1.65E+02	6.93E+01	1.65E+02	6.63E+01	1.14E+02	5.59E+01	1.14E+02	8.00E+01	1.16E+02	6.10E+01	1.40E+02	1.03E+02	1.53E+02
Acrolein	1.30E-02	5.22E-02	1.30E-02	5.22E-02	1.30E-02	5.22E-02	2.45E+03	8.28E+03	1.36E+03	3.98E+03	1.36E+03	3.83E+03	2.75E+03	6.99E+03	2.25E+03	6.99E+03	3.21E+03	7.22E+03	2.56E+03	6.39E+03	4.23E+03	8.56E+03
Acrylonitrile	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	2.41E+00	9.43E+00	5.29E+00	1.56E+01	5.52E+00	1.57E+01	3.01E+00	1.02E+01	2.41E+00	1.02E+01	4.25E+00	1.20E+01	3.43E+00	1.05E+01	5.57E+00	1.21E+01
Benzene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	1.03E+00	2.72E+00	1.16E+00	2.86E+00	1.20E+00	2.93E+00	8.77E-01	2.67E+00	7.97E-01	2.67E+00	1.09E+00	2.84E+00	9.78E-01	2.93E+00	1.33E+00	2.18E+00
Crotonaldehyde	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	9.10E-01	5.47E+00	1.16E+00	4.17E+00	1.23E+00	4.09E+00	1.35E+00	4.70E+00	1.10E+00	4.70E+00	2.01E+00	4.59E+00	1.20E+00	3.99E+00	2.47E+00	5.69E+00
Formaldehyde	1.09E-04	6.86E-04	1.13E-04	8.27E-04	1.09E-04	6.86E-04	2.27E+00	8.01E+00	5.81E-01	1.56E+00	5.46E-01	1.42E+00	1.90E+00	9.94E+00	2.26E+00	9.94E+00	2.82E+00	8.42E+00	1.71E+00	4.66E+00	3.70E+00	9.66E+00
Toluene	1.59E-08	6.35E-08	1.59E-08	6.35E-08	1.59E-08	6.35E-08	9.46E-03	2.82E-02	1.11E-02	3.24E-02	1.11E-02	3.28E-02	9.31E-03	2.76E-02	8.10E-03	2.76E-02	1.19E-02	3.00E-02	1.05E-02	3.53E-02	1.52E-02	2.50E-02
Sum HQ	1.33E-02	5.39E-02	1.33E-02	5.43E-02	1.33E-02	5.39E-02	2.51E+03	8.49E+03	1.44E+03	4.17E+03	1.44E+03	4.02E+03	2.82E+03	7.13E+03	2.31E+03	7.13E+03	3.30E+03	7.37E+03	2.63E+03	6.56E+03	4.35E+03	8.74E+03

COMPARATIVE NON-CANCER RISK ASSESSMENT OF GLAS ENDS PRODUCTS COMPARED TO COMBUSTED CIGARETTE

	Glas ENDS Relative to Tobacco Cigarettes											
	HQ Ratio (Cumulative)						% Reduction of Non-Cancer Risk (Cumulative HQ)					
	Blonde Tobacco (50 mg/mL)		Fresh Menthol (50 mg/mL)		Gold (50 mg/mL)		Blonde Tobacco (50 mg/mL)		Fresh Menthol (50 mg/mL)		Gold (50 mg/mL)	
	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense
3R4F	5.28E-06	6.34E-06	5.29E-06	6.39E-06	5.28E-06	6.34E-06	99.999	99.999	99.999	99.999	99.999	99.999
VLN Regular King	5.28E-06	1.29E-05	9.27E-06	1.35E-05	9.25E-06	1.29E-05	99.999	99.999	99.999	99.999	99.999	99.999
VLN Menthol King	9.23E-06	1.34E-05	9.25E-06	1.35E-05	9.23E-06	1.34E-05	99.999	99.999	99.999	99.999	99.999	99.999
Marlboro Gold King Box	4.71E-06	7.55E-06	4.72E-06	7.61E-06	4.71E-06	7.55E-06	100.000	99.999	100.000	99.999	100.000	99.999
Marlboro Menthol Gold King Soft Pack	5.74E-06	7.55E-06	5.76E-06	7.61E-06	5.74E-06	7.55E-06	100.000	99.999	99.999	99.999	99.999	99.999
Marlboro Red King Soft Pack	4.02E-06	7.31E-06	4.03E-06	7.37E-06	4.02E-06	7.31E-06	100.000	99.999	100.000	99.999	100.000	99.999
Camel Blue King	5.05E-06	8.22E-06	5.06E-06	8.28E-06	5.05E-06	8.22E-06	99.999	99.999	99.999	99.999	99.999	99.999
Newport Menthol Green King	3.05E-06	6.16E-06	3.06E-06	6.21E-06	3.05E-06	6.16E-06	100.000	99.999	100.000	99.999	100.000	99.999

QUANTITATIVE CANCER RISK ASSESSMENT OF GLAS ENDS PRODUCTS EMISSION CONSTITUENTS COMPARED TO COMBUSTED CIGARETTE

CANCER RISK (ILCR)																						
HPHC	GLAS PRODUCTS						REF. CIGARETTE		MARKET CIGARETTE													
	Blonde Tobacco (50 mg/mL)		Fresh Menthol (50 mg/mL)		Gold (50 mg/mL)		3R4F		VLN Regular King		VLN Menthol King		Marlboro Gold King Box		Marlboro Menthol Gold King Soft Pack		Marlboro Red King Soft Pack		Camel Blue King		Newport Menthol Green King	
	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense
Acetaldehyde	2.59E-09	2.01E-08	3.04E-09	2.53E-08	3.79E-09	3.48E-08	1.21E-03	3.72E-03	1.31E-03	3.27E-03	1.37E-03	3.27E-03	1.31E-03	2.27E-03	1.11E-03	2.27E-03	1.58E-03	2.29E-03	1.21E-03	2.78E-03	2.03E-03	3.03E-03
Acrylonitrile	0.00E+00	0.00E+00	0.00E+00	0.00E+00	3.08E-09	0.00E+00	3.27E-04	1.28E-03	7.19E-04	2.12E-03	7.51E-04	2.13E-03	4.10E-04	1.38E-03	3.27E-04	1.38E-03	5.78E-04	1.63E-03	4.67E-04	1.43E-03	7.57E-04	1.64E-03
Benzene	0.00E+00	0.00E+00	0.00E+00	0.00E+00	5.31E-10	2.12E-09	2.41E-04	6.37E-04	2.71E-04	6.68E-04	2.81E-04	6.85E-04	2.05E-04	6.24E-04	1.87E-04	6.24E-04	2.56E-04	6.65E-04	2.29E-04	6.85E-04	3.11E-04	5.11E-04
Formaldehyde	1.41E-08	8.92E-08	1.47E-08	1.08E-07	2.04E-08	1.71E-07	2.95E-04	1.04E-03	7.56E-05	2.03E-04	7.09E-05	1.84E-04	2.48E-04	1.29E-03	2.94E-04	1.29E-03	3.67E-04	1.09E-03	2.22E-04	6.06E-04	4.81E-04	1.26E-03
Crotonaldehyde	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	2.98E-04	1.79E-03	3.79E-04	1.36E-03	4.03E-04	1.34E-03	4.42E-04	1.54E-03	3.61E-04	1.54E-03	6.59E-04	1.50E-03	3.91E-04	1.31E-03	8.09E-04	1.86E-03
Sum ILCR	1.67E-08	1.09E-07	1.77E-08	1.33E-07	2.78E-08	2.08E-07	2.37E-03	8.47E-03	2.75E-03	7.63E-03	2.88E-03	7.62E-03	2.62E-03	7.10E-03	2.28E-03	7.10E-03	3.45E-03	7.17E-03	2.52E-03	6.80E-03	4.39E-03	8.30E-03

COMPARATIVE CANCER RISK ASSESSMENT OF GLAS ENDS PRODUCTS COMPARED TO COMBUSTED CIGARETTE

	Glas ENDS Relative to Tobacco Cigarettes												
	ILCR Ratio (Cumulative)						% Reduction of Cancer Risk (Cumulative ILCR)						
	Blonde Tobacco (50 mg/mL)		Fresh Menthol (50 mg/mL)		Gold (50 mg/mL)			Blonde Tobacco (50 mg/mL)		Fresh Menthol (50 mg/mL)		Gold (50 mg/mL)	
	Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense		Non-Intense	Intense	Non-Intense	Intense	Non-Intense	Intense
Tobacco Cigarette													
3R4F	7.05E-06	1.29E-05	7.48E-06	1.57E-05	1.17E-05	2.45E-05		99.999	99.999	99.999	99.998	99.999	99.998
VLN Regular King	6.07E-06	1.43E-05	6.43E-06	1.74E-05	1.01E-05	2.72E-05		99.999	99.999	99.999	99.998	99.999	99.997
VLN Menthol King	5.81E-06	1.43E-05	6.16E-06	1.74E-05	9.66E-06	2.73E-05		99.999	99.999	99.999	99.998	99.999	99.997
Marlboro Gold King Box	6.38E-06	1.54E-05	6.77E-06	1.87E-05	1.06E-05	2.92E-05		99.999	99.998	99.999	99.998	99.999	99.997
Marlboro Menthol Gold King Soft Pack	7.34E-06	1.54E-05	7.79E-06	1.87E-05	1.22E-05	2.92E-05		99.999	99.998	99.999	99.998	99.999	99.997
Marlboro Red King Soft Pack	4.85E-06	1.52E-05	5.14E-06	1.85E-05	8.07E-06	2.89E-05		100.000	99.998	99.999	99.998	99.999	99.997
Camel Blue King	6.64E-06	1.61E-05	7.04E-06	1.95E-05	1.10E-05	3.05E-05		99.999	99.998	99.999	99.998	99.999	99.997
Newport Menthol Green King	3.81E-06	1.32E-05	4.04E-06	1.60E-05	6.33E-06	2.50E-05		100.000	99.999	100.000	99.998	99.999	99.997

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