

Complete or partial switching from combustible cigarettes to the RELX Infinity electronic nicotine delivery system (ENDS) over 8 weeks results in lower exposure to harmful and potentially harmful constituents (HPHCs) found in cigarette smoke

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CHEERAIN

Risk Reduction



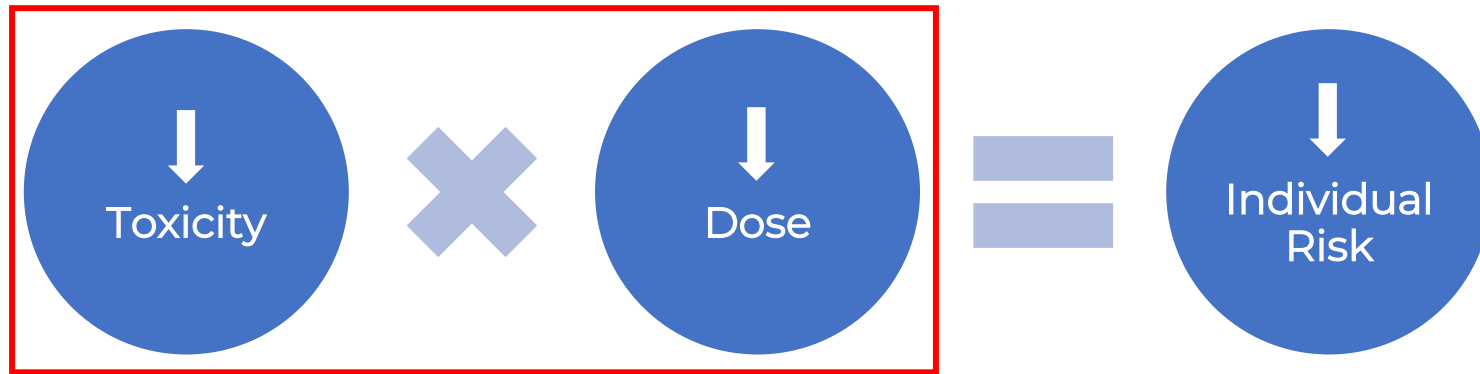
Combustible Cigarettes

Heated Tobacco Products

Traditional Smokeless Tobacco Products

Vapor/Modern Oral Nicotine Products

Medicinal Products



Study Disclosures

Study Sponsor	Cheerain HK Limited
Study Sites	Alliance for Multispecialty Research – Knoxville, TN Alliance for Multispecialty Research – Lexington, KY Alliance for Multispecialty Research – Las Vegas, NV Pillar Clinical Research – Bentonville, AR Bio-Kinetic Clinical Applications – Springfield, MO
Bioanalysis	Celerion
Statistical Analysis	Celerion
Ethics Approval	Advara IRB
Study Registration	Clinicaltrials.gov - NCT04708106
Disclaimer	The results and conclusions presented herein are intended for scientific discussion purposes only.

Study Design

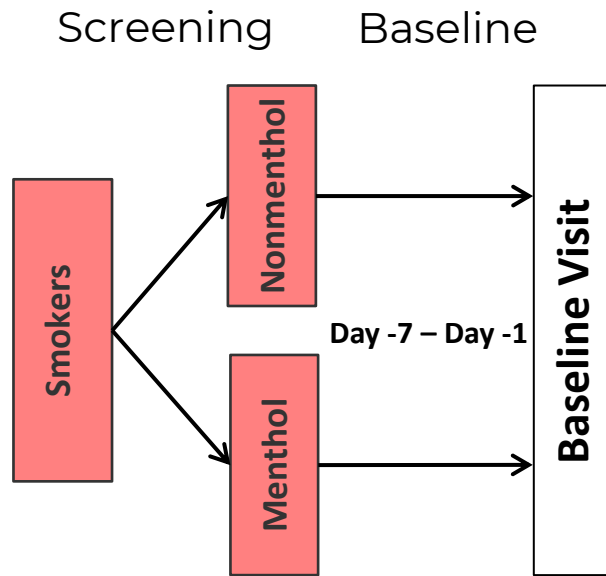
Study Description Randomized, 8-week, open-label, parallel-cohort switching study of healthy adult smokers

Study Products RELX Infinity ENDS

- Two-piece, pod-based closed system
- Rechargeable 6.5 W battery
- Nonrefillable 1.9 mL pod
- Tobacco or menthol flavored e-liquids with 4% nicotine (salt) and a PG:VG ratio of ~40:60

Usual brand combustible cigarettes

Study Design



Subject Population

- Healthy adult smokers 22 to 65 years of age
- Typically smoked ≥ 5 cigarettes per day and typically smoked daily for ≥ 1 year
- No ENDS use on > 7 days during each of the 3 months prior to Screening
- Not postponing a planned smoking quit attempt in order to participate

Baseline Period

- Usual smoking behaviors through the Baseline Visit
 - Endpoint measurements:
 - Self-reported cigarette use during 7-day baseline period
 - Changes in biomarkers of exposure
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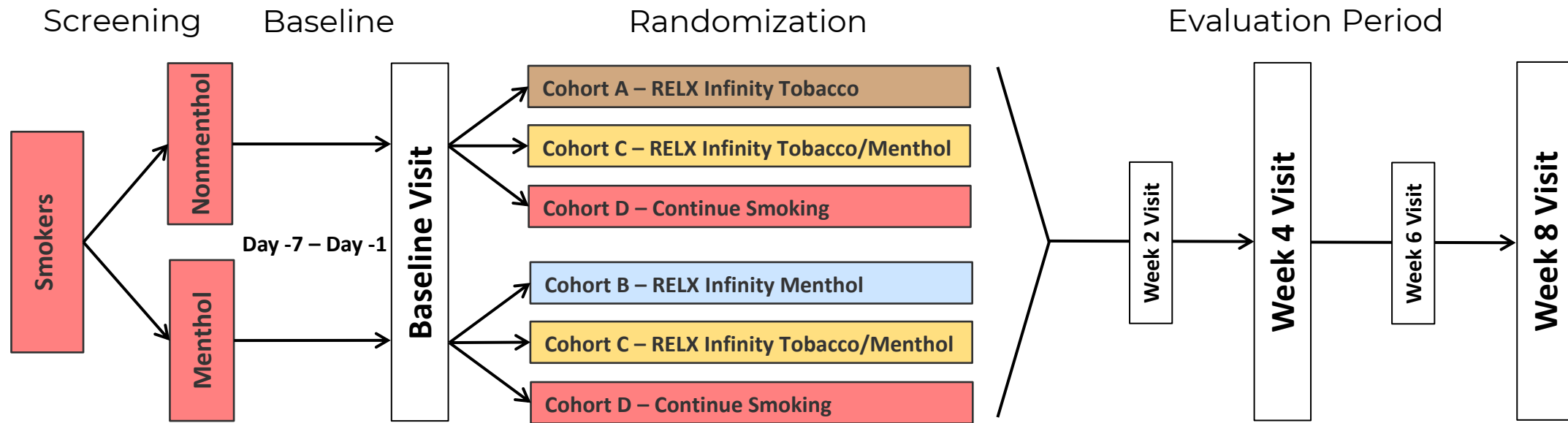
Biomarkers of Exposure

	Biomarker	Exposure Constituent	Toxicity Class
Breath	Carbon monoxide	Carbon monoxide	RDT
	NNAL	NNK	CA
	NNN	NNN	CA
	3-HPMA	Acrolein	CT, RT
	CEMA	Acrylonitrile	CA, RT
	HMPMA	Crotonaldehyde	CA
Urine*	S-PMA	Benzene	CA, CT, RDT
	HEMA	Ethylene oxide	CA, RDT, RT
	1-OHP	Pyrene (PAH)	CA
	o-Toluidine	Toluidine (AA)	CA
	Nicotine equivalents	Nicotine	AD, RDT
	Propylene glycol	Propylene glycol	

* At-home overnight collections; biomarker concentrations were normalized to urine creatinine concentration.

1-OHP = 1-hydroxypyrene, 3-HPMA = 3-hydroxypropylmercapturic acid, AA = aromatic amines, AD = addictive, CA = carcinogen, CEMA = 2-cyanoethyl-mercapturic acid, CT = cardiovascular toxicity, HEMA = hydroxyethyl mercapturic acid, HMPMA = 3-hydroxy-1-methylpropylmercapturic acid, NNAL = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol, NNK= 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone), NNN = N-nitrosornornicotine, PAH = polycyclic aromatic hydrocarbons, RDT = reproductive or developmental toxicant, RT = respiratory toxicant, S-PMA = S-phenyl mercapturic acid

Study Design



Randomization

- Based on usual brand cigarette flavor

Evaluation Period

- RELX Infinity cohorts were instructed to switch completely from cigarettes as quickly as possible
- Endpoint measurements
 - Daily self-reported RELX Infinity pod and cigarette use
 - Biomarkers of exposure at Week 4 and Week 8

Analysis Populations

Full Analysis Population (planned)

- Primary analysis population (all subjects)

Per Protocol Population (planned)

- “Complete switch”
 - Primary requirements (RELX cohorts)
 - Self-reported $\geq 90\%$ CPD reduction from baseline
 - Urine cotinine > 200 ng/mL (each visit)
 - Exhaled carbon monoxide ≤ 8 ppm (each visit)
 - Urine NNAL reduction from baseline $\geq 65\%$ (Week 4 and Week 8)
 - Separate populations for Week 4 and Week 8
 - Data summarized by cohort
-

Dual Use Exploratory Population (post hoc)

- “Partial switch”
 - Subjects who were not included in the Week 4 or Week 8 per protocol populations
 - RELX cohort data combined for summaries
-

Subject Characteristics

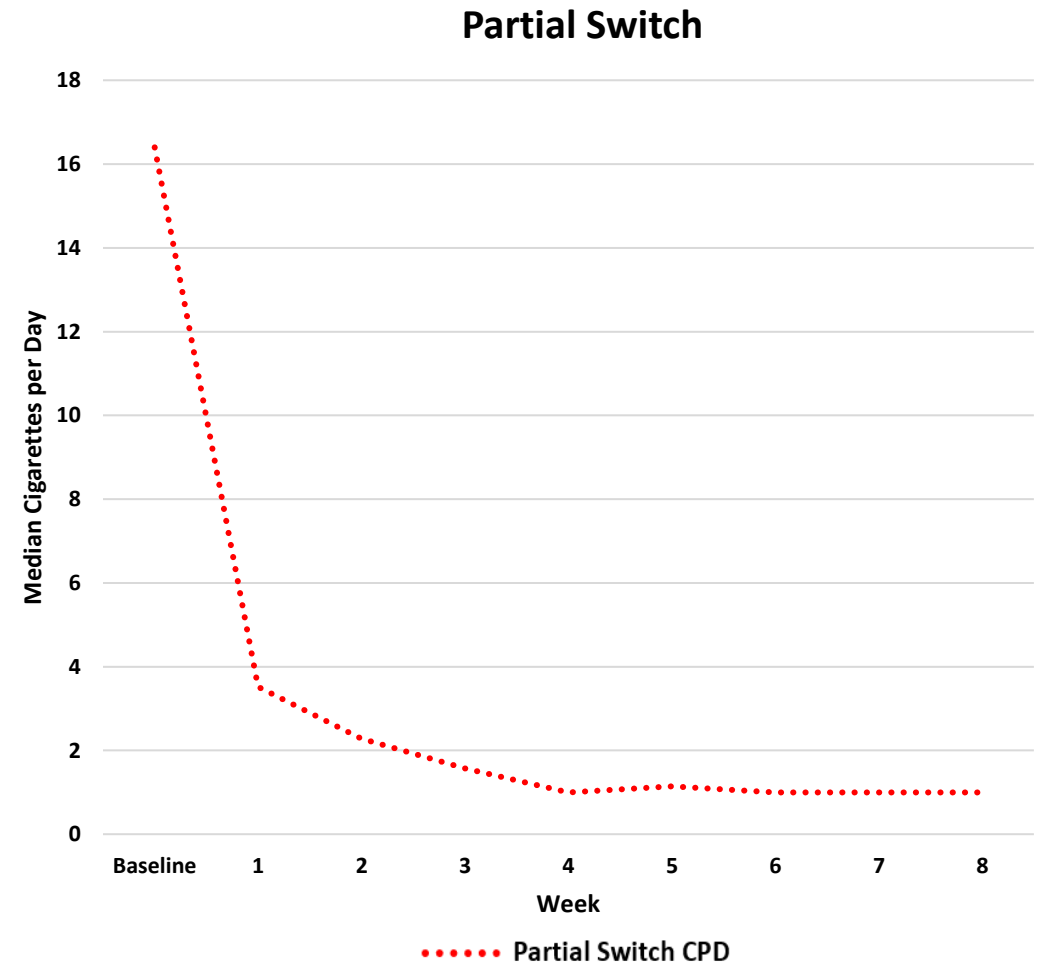
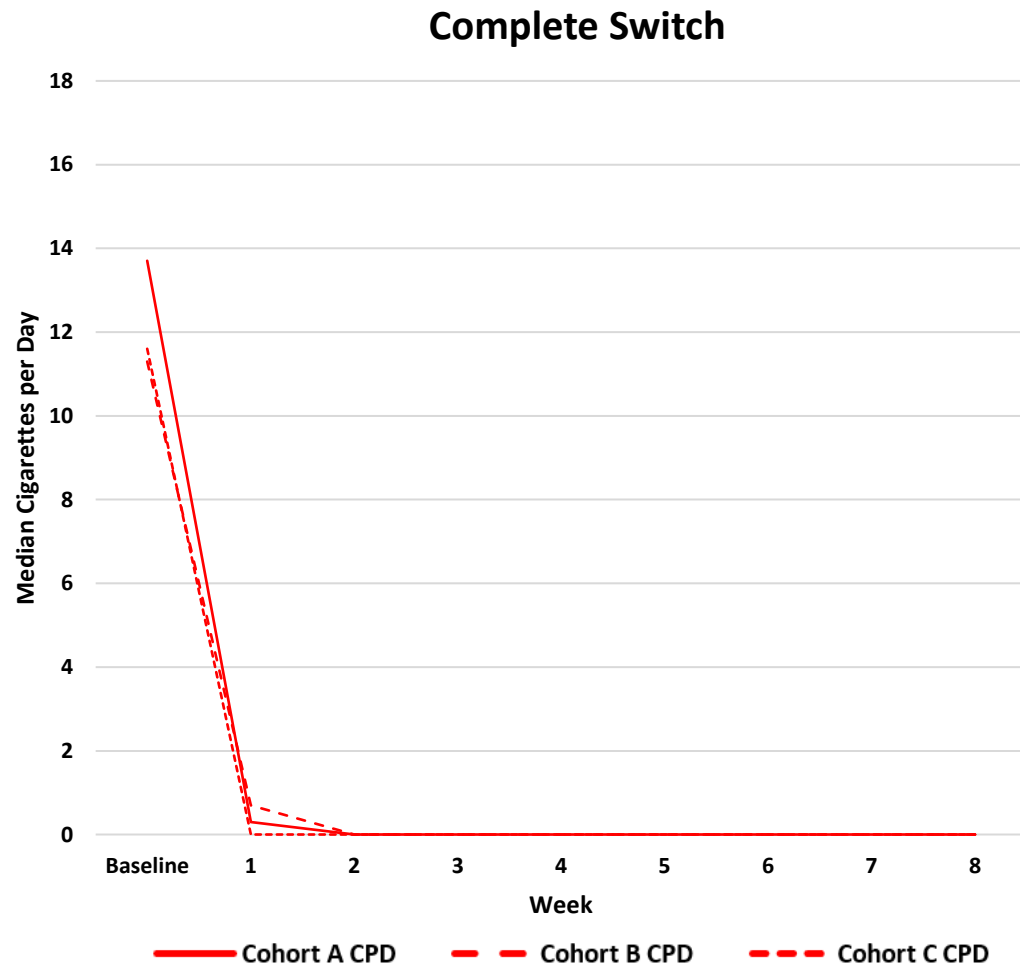
Enrolled/Completed/Full Analysis Set	N	194/170/191
Sex	Female [n(%)]	79 (41.4%)
	Male [n(%)]	112 (58.6%)
Race	White or Caucasian [n(%)]	163 (85.3%)
	Black or African American [n(%)]	23 (12.0%)
	Other [n(%)]	5 (2.7%)
Age (years)	Mean (SD)	42.1 (10.5)
Usual Brand Cigarette Flavor	Nonmenthol [n(%)]	102 (53.4%)
	Menthol [n(%)]	89 (46.6%)
Smoking History (years)	Mean (SD)	23.4 (11.9)
Cigarettes per Day	Mean (SD)	16.4 (7.6)
Penn State Cigarette Dependence Index	Mean (SD)	12.1 (3.3)

Analysis Populations

		Cohort			
		A	B	C	D
Full Analysis Population		62	54	53	22
Per Protocol Population (complete switch)	Week 4	17 (27%)	12 (22%)	19 (36%)	20 (91%)
	Week 8	18 (29%)	15 (28%)	18 (34%)	20 (91%)
Dual Use Exploratory Population (partial switch)	Week 4	————— 104 —————			
	Week 8	————— 99 —————			

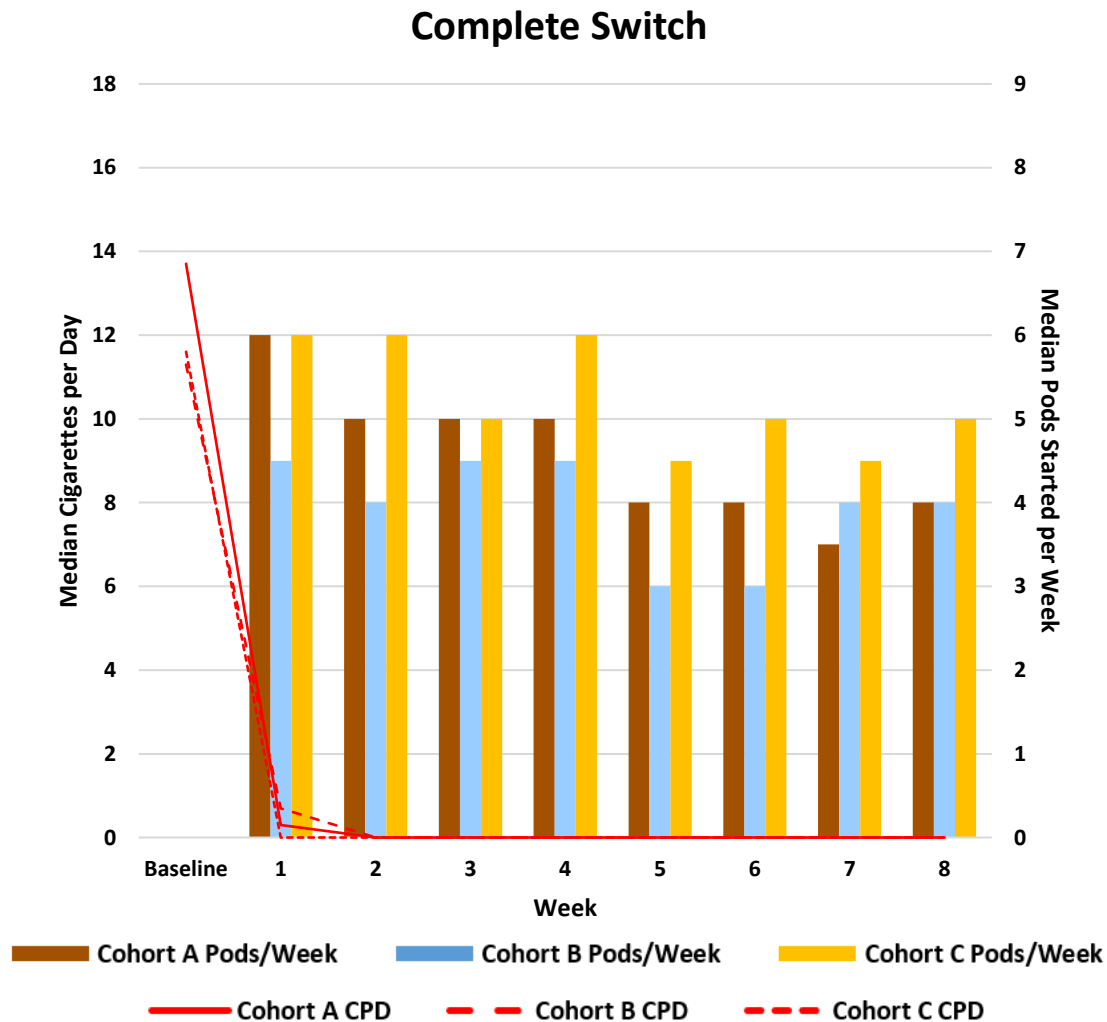
Cohort A: RELX Infinity tobacco flavor
 Cohort B: RELX Infinity menthol flavor
 Cohort C: RELX Infinity tobacco and menthol flavor
 Cohort D: Continue smoking

Self-Reported Cigarette Use

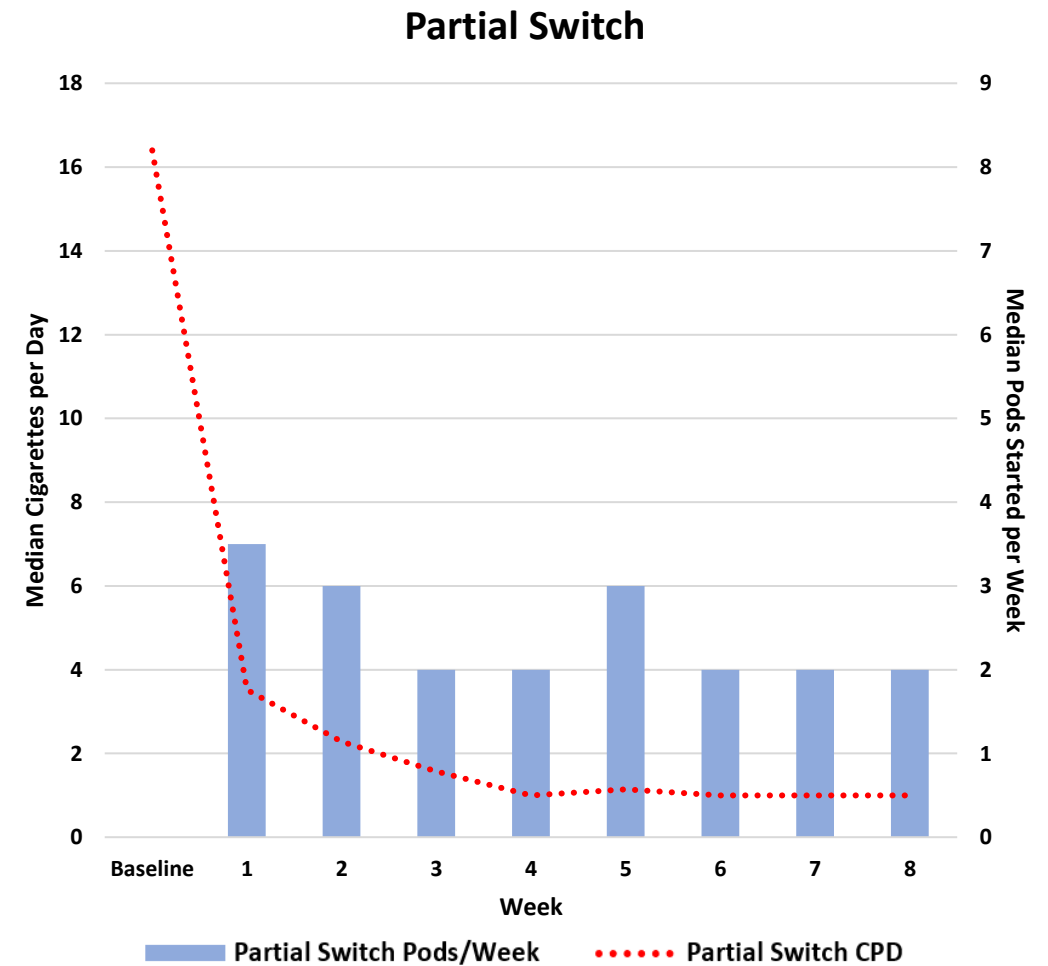


Cohort A: RELX Infinity tobacco flavor
Cohort B: RELX Infinity menthol flavor
Cohort C: RELX Infinity tobacco and menthol flavor

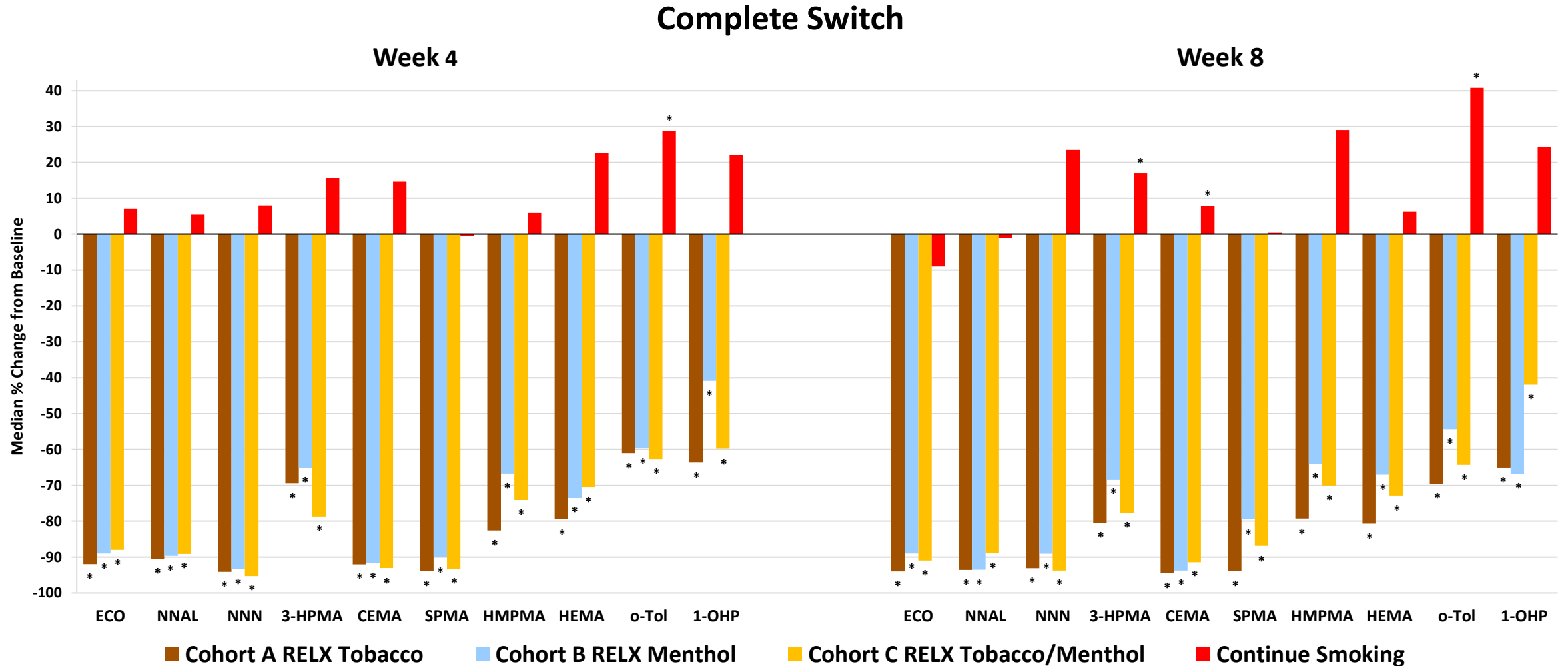
Self-Reported RELX Product Use



Cohort A: RELX Infinity tobacco flavor
 Cohort B: RELX Infinity menthol flavor
 Cohort C: RELX Infinity tobacco and menthol flavor



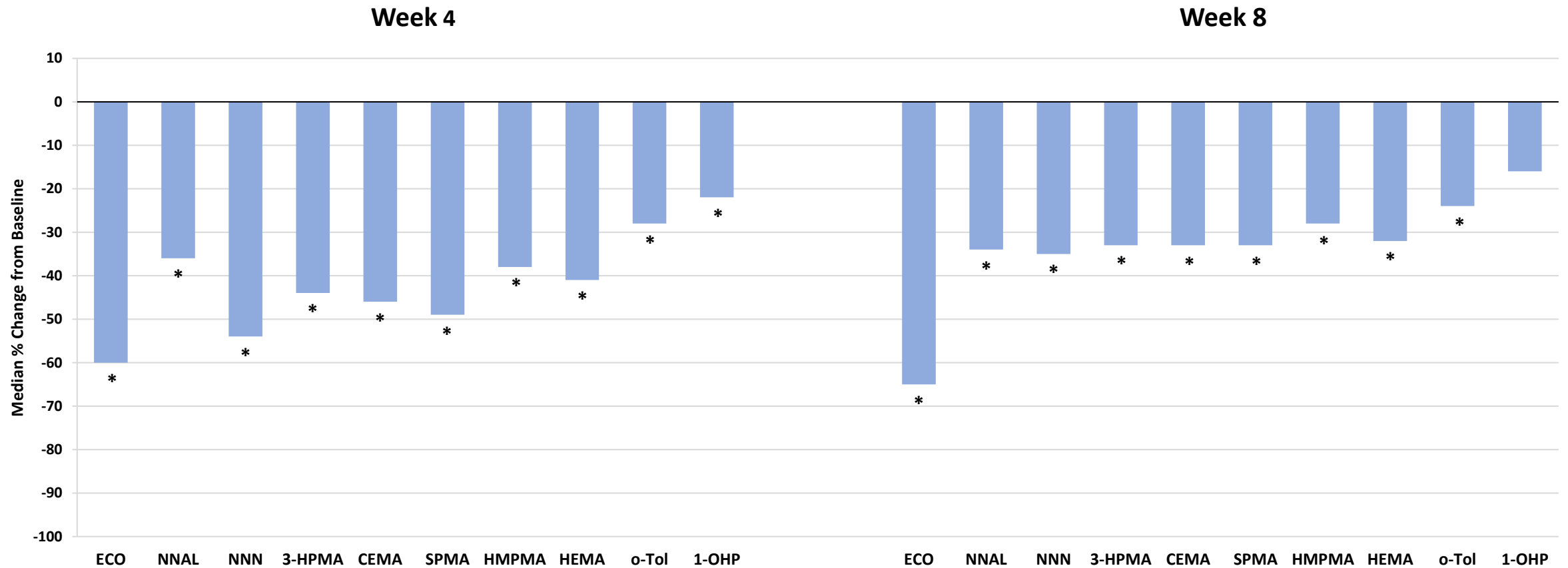
Changes in Biomarkers of Exposure



*Indicates significant difference from baseline by the Wilcoxon Signed Rank test ($p < 0.05$).

Changes in Biomarkers of Exposure

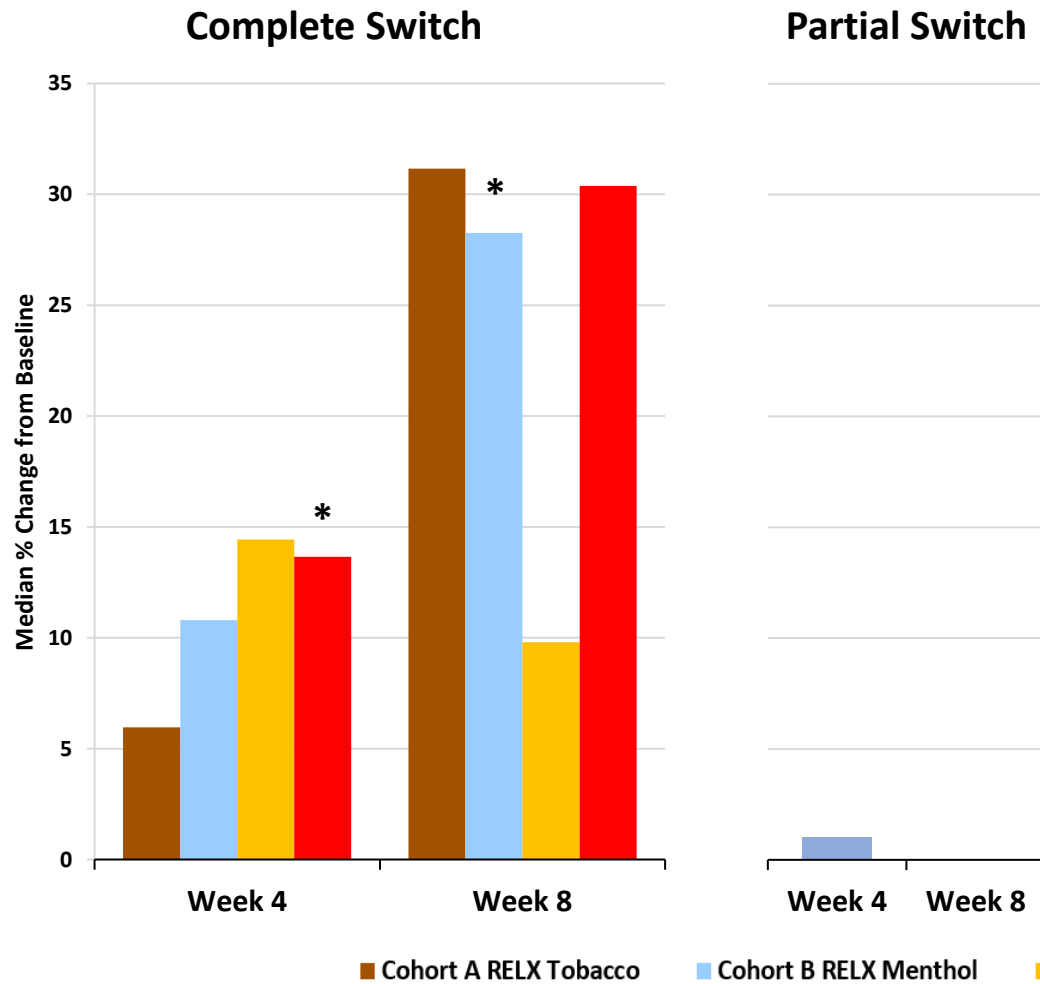
Partial Switch



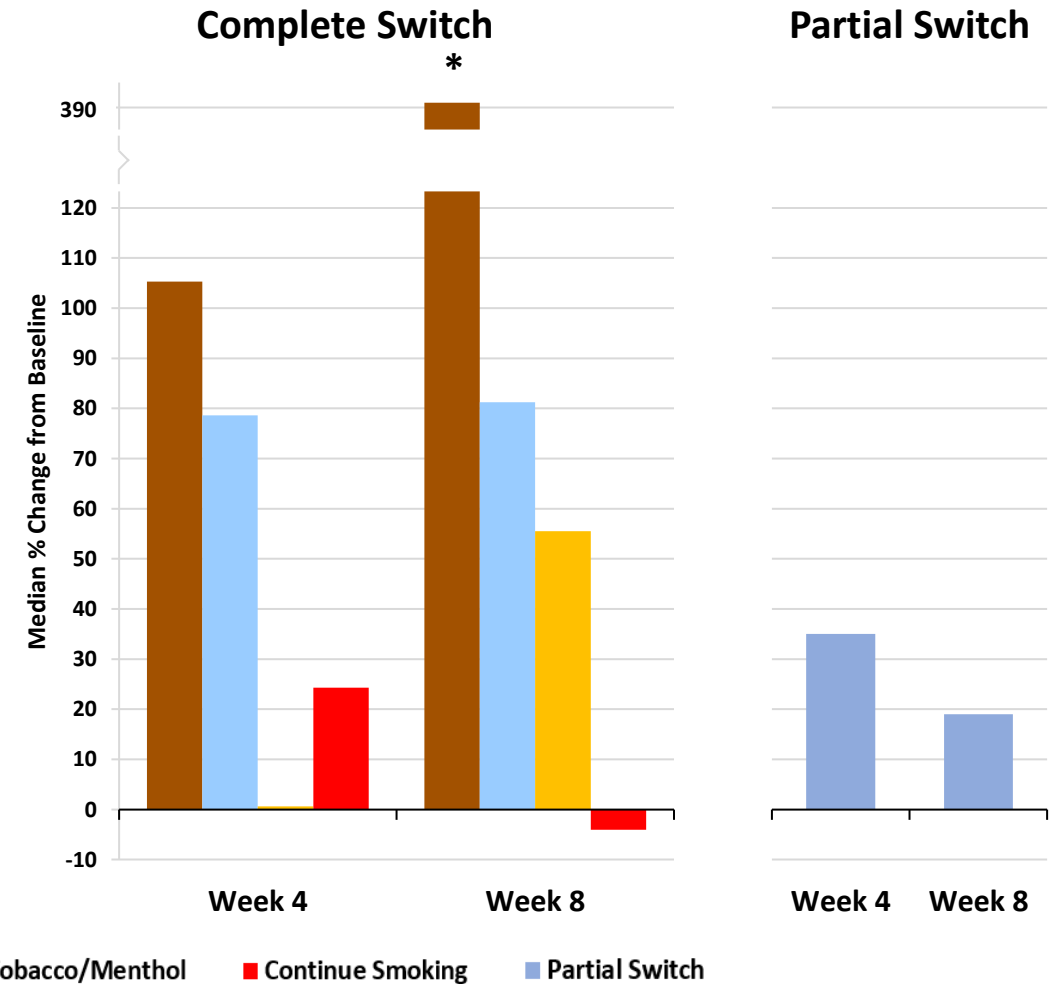
*Indicates significant difference from baseline by the Wilcoxon Signed Rank test ($p < 0.05$).

Changes in Biomarkers of Exposure

Nicotine Equivalents



Propylene Glycol



*Indicates significant difference from baseline by the Wilcoxon Signed Rank test ($p < 0.05$).

Conclusions

- Subjects who completely or partially switched from cigarettes to the RELX Infinity ENDS experienced significant reductions in biomarkers of exposure to HPHCs found in cigarette smoke with links to cancer, cardiovascular disease, respiratory disease, and reproductive and developmental toxicity.
- Complete switching from combustible cigarettes to the RELX Infinity ENDS resulted in a larger reduction compared to partially switching.
- Increases from baseline in propylene glycol and nicotine were typically observed following complete and partial switching though not all changes were statistically significant.
- While these observations contribute to the growing body of evidence suggesting that ENDS have the potential to provide harm reduction relative to combustible cigarettes, long-term studies are necessary to understand whether these changes will have a positive impact on disease.

Acknowledgements

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Pillar Clinical Research

Bio-Kinetic Clinical Applications