Individual exposure levels in subjects switching to a Tobacco Heating Product for 5 days

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ENDS UK | London, United Kingdom | 6th June 2019

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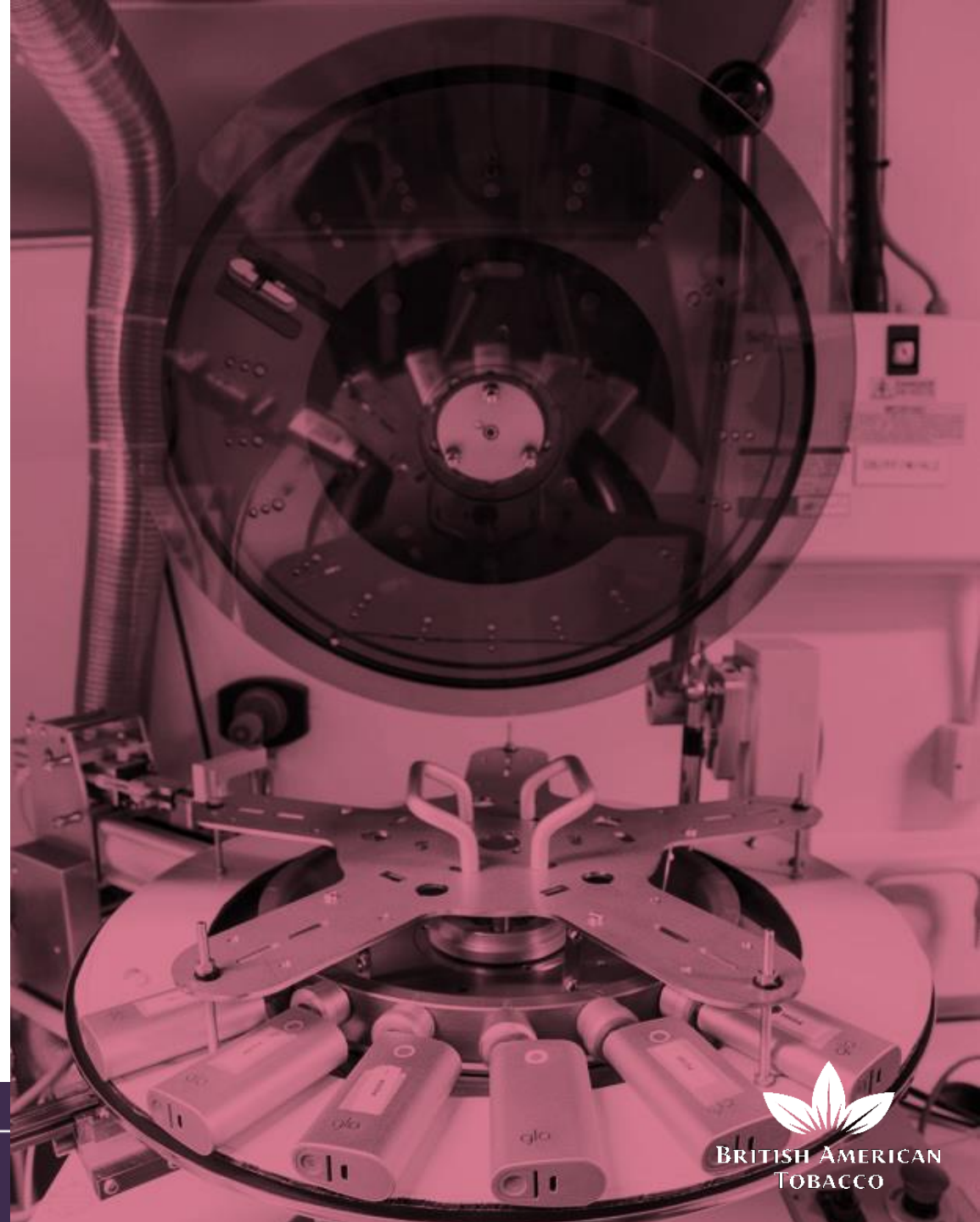
Disclosures

I declare that this work was fully funded by British American Tobacco (BAT) and I am a full-time employee of British American Tobacco (Investments) Ltd. BAT develops, manufactures and sells tobacco and nicotine products around the world.

Agenda

- Investigational product/Risk Assessment Framework
- Study Objectives
- Study Design
- Biomarkers of Exposure (BoE)
- Results
- Summary



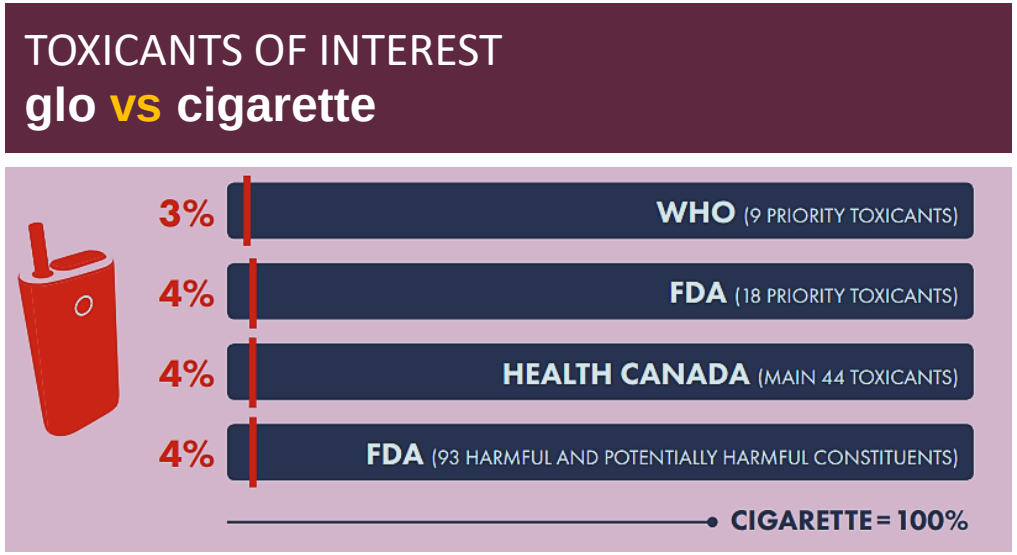
glo THP

Tobacco Neostik, single use and disposable

Heats to ~240°C sufficient to release nicotine & flavours without combustion

Battery-operated and recharged by micro USB

Emissions show much-reduced toxicant levels compared to cigarettes*



*These qualities do not necessarily mean this product produces less adverse health effects than tobacco products

Forster M. *et al.* (2017). Regul Toxicol Pharmacol. 93:14-13

Our Framework
to Establish Reduced Risk Potential

Purpose	Type of Studies	glo
Population risk reduction	Post-market surveillance	✓
	Consumer perception study	✓
Individual risk reduction	Systems science	✓
	Biomarker of effect study	In progress
Toxicant exposure reduction	*In vitro* models of disease	✓
	Exposure & pharmacokinetic studies	✓
	Computational toxicology	✓
Stewardship science	In vitro regulatory toxicology	✓
	Chemical & physical characterisation	✓
	Product design stability	✓

Murphy J. *et al.* (2017). Regul Toxicol Pharmacol.

Study Title

A Randomised Controlled Single-Centre Open-Label Study in Healthy Subjects to Evaluate the Effect on Biomarkers of Exposure (BoE) of Switching from a Combustible Cigarette to a Potentially Reduced Risk Product

Study Objectives

To quantitatively assess within-arm changes in Biomarkers of Exposure (BoE) and Biomarkers of Biological Effect (BoBE) when smokers switch to glo THP or cessation

Ethical & Regulatory Considerations

ORECNI

Office for Research Ethics Committees Northern Ireland (ORECNI; ref.: 17/NI/0065)

Ethics

ISRCTN registry

Registry number: ISRCTN80651909

Registration

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Study Conduct

Study Location: Belfast, United Kingdom

Study Population

Age & Gender

Healthy male or female smokers, aged 21 – 55 years

- Smoking status verified by urinary cotinine and eCO at Screening and Admission
- Healthy status verified by vital signs, clinical laboratory evaluations, physical examination, ECG and lung function tests

Smoking History

Typically smoke 10 – 30 FMCs per day, within 6 – 8 mg ISO tar bands

- Min. 6 month use of current brand and 3 years smoking history, prior to Screening

Main Exclusion Criteria

Planning to quit smoking in next 12 months

- Regular use of nicotine or tobacco products other than FMCs
- Non-inhalers (self-reported or observed at Admission)

Biomarkers of Exposure (BoE)

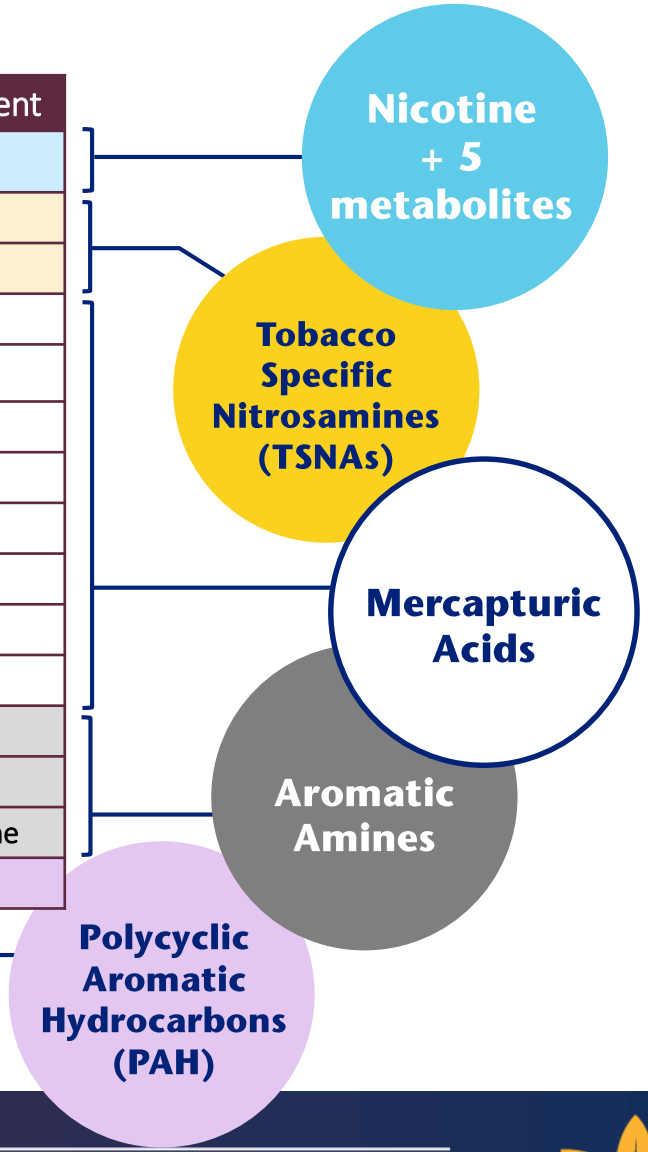
Exhaled breath

- Carbon monoxide (eCO)

Urine

- Urinary biomarkers

Biomarker	Smoke Constituent
Total Nicotine equivalents	Nicotine
Total NNAL	NNK
Total NNN	NNN
3-HPMA	Acrolein
HMPMA	Crotonaldehyde
S-PMA	Benzene
MHBMA	1,3-Butadiene
CEMA	Acrylonitrile
HEMA	Ethylene oxide
AAMA	Acrylamide
GAMA	Acrylamide
4-ABP	4-Aminobiphenyl
o-Tol	o-Toluidine
2-AN	2-Aminonaphthalene
1-OHP	Pyrene

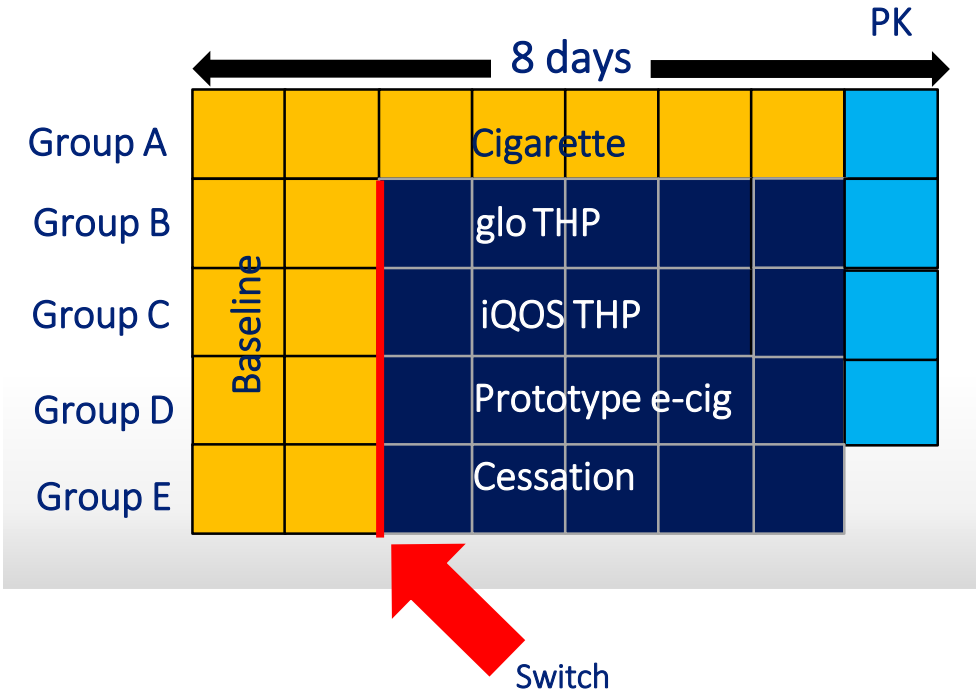


Study Design

- A single-centre, randomised, open label, 5-arm, 5-day *ad libitum* Exposure study during 8-day confinement

- Nicotine PK at end of confined switching period, during defined single-use session

- 30 subjects in each of the study groups = 150 subjects



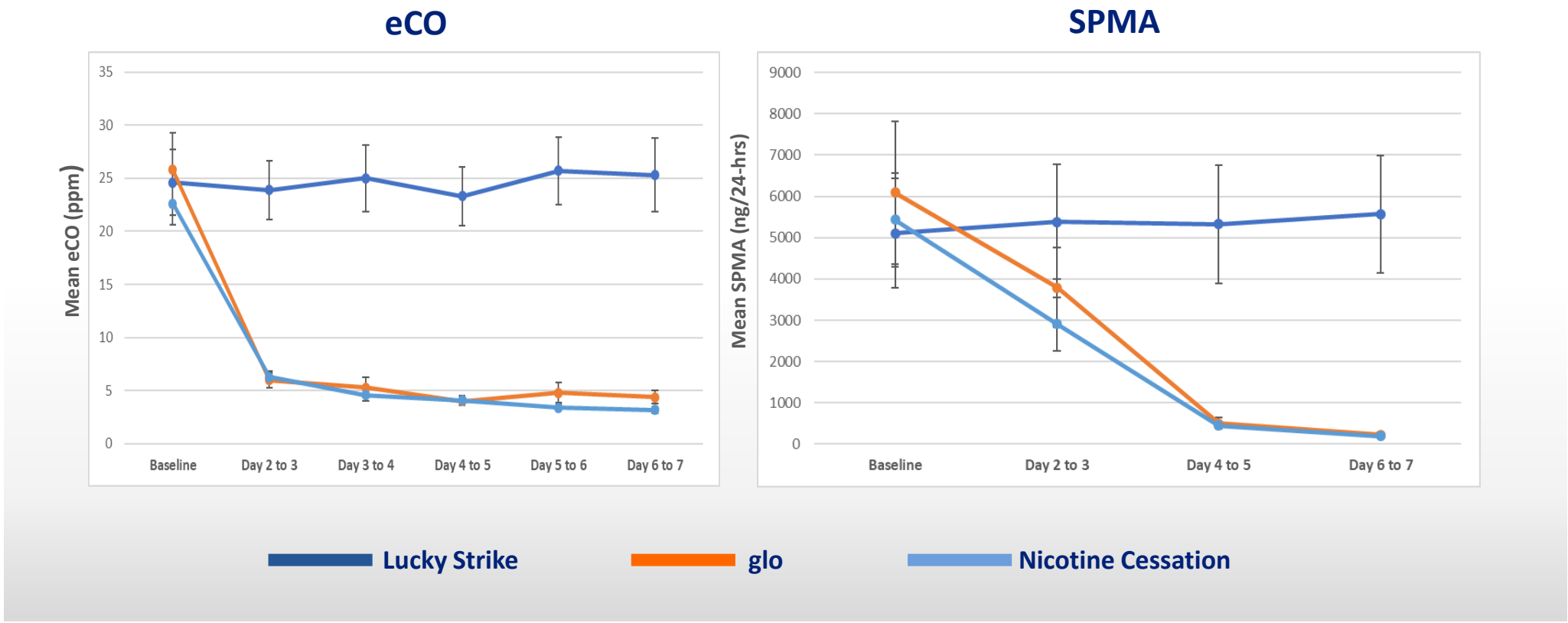
Study Design

- ***Ad libitum*** **use of all products in study (max. 120% of self-reported CPD) excluding cessation group from days 3 to 7**

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
24-hour urine sample		X	X		X		X	
Exhaled CO (eCO)	X	X	X	X	X	X	X	
Blood sample		X			X		X	
Nicotine Pharmacokinetics (PK)								X

Results

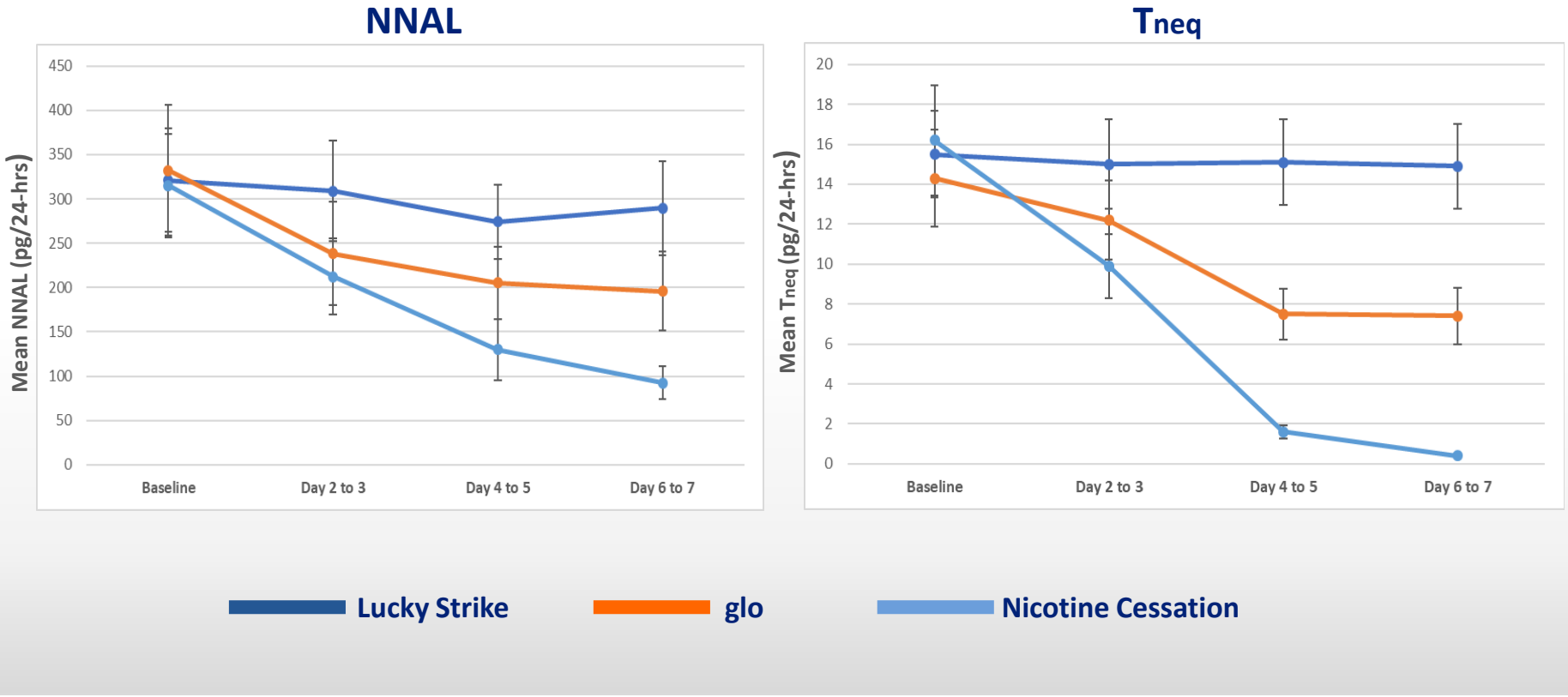
Significant reductions in eCO and SPMA following switch*



*These qualities do not necessarily mean this product produces less adverse health effects than tobacco products

Results

- Significant reductions in NNAL following switch
- Total Nicotine remained high, but flat following switch to glo THP*



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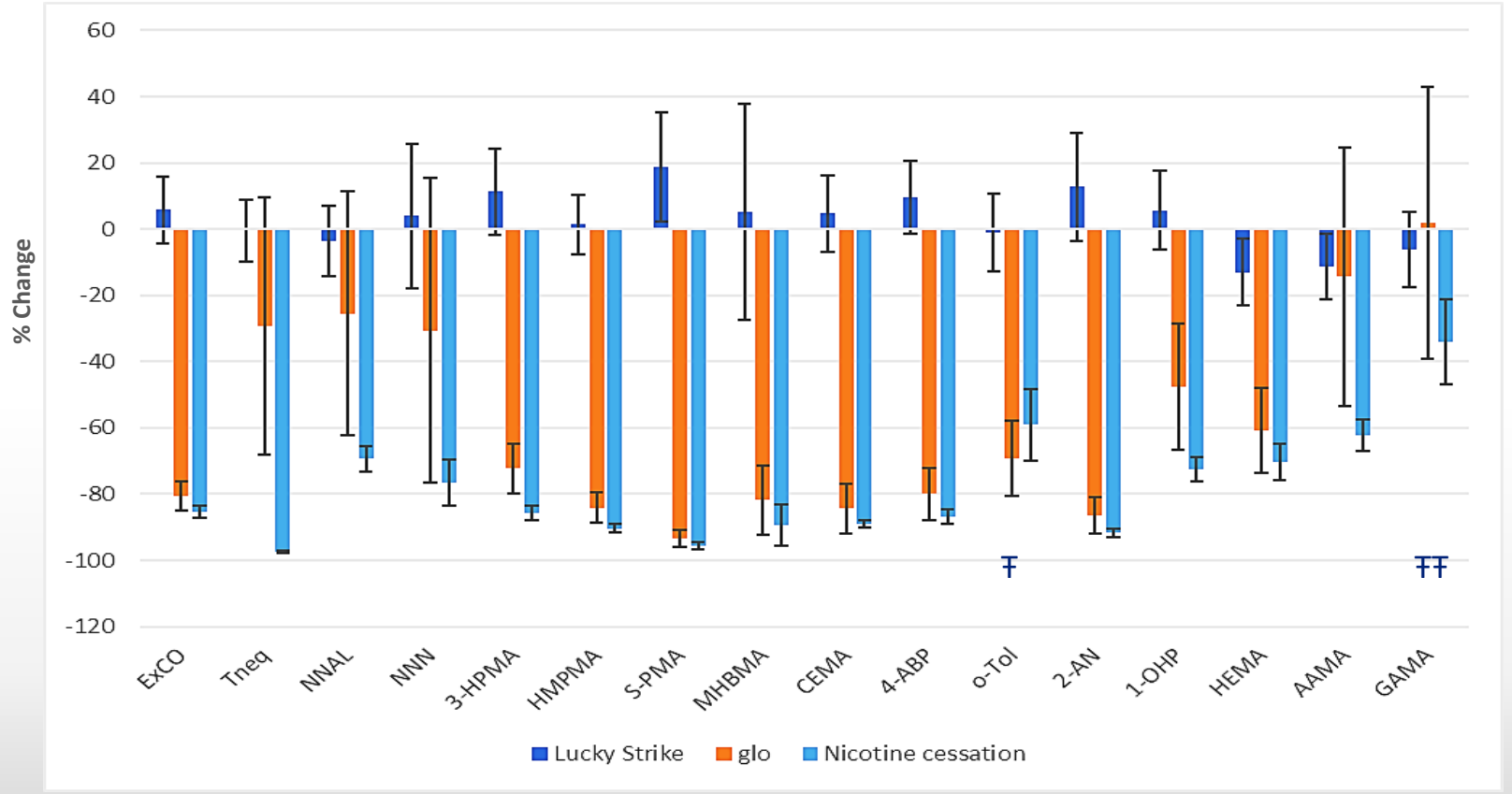
Results

Generally, levels of BoE significantly reduced following switch*

Mean excretion on Day 6 to 7 vs excretion at Baseline



Ŧ O-Tol sensitivity analysis with one subject value removed from cessation group. With this value included cessation shows an increase of 274.7%

ŦŦ GAMA showed significant reductions in the glo group when Holm's adjustment for multiplicity was applied

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Summary

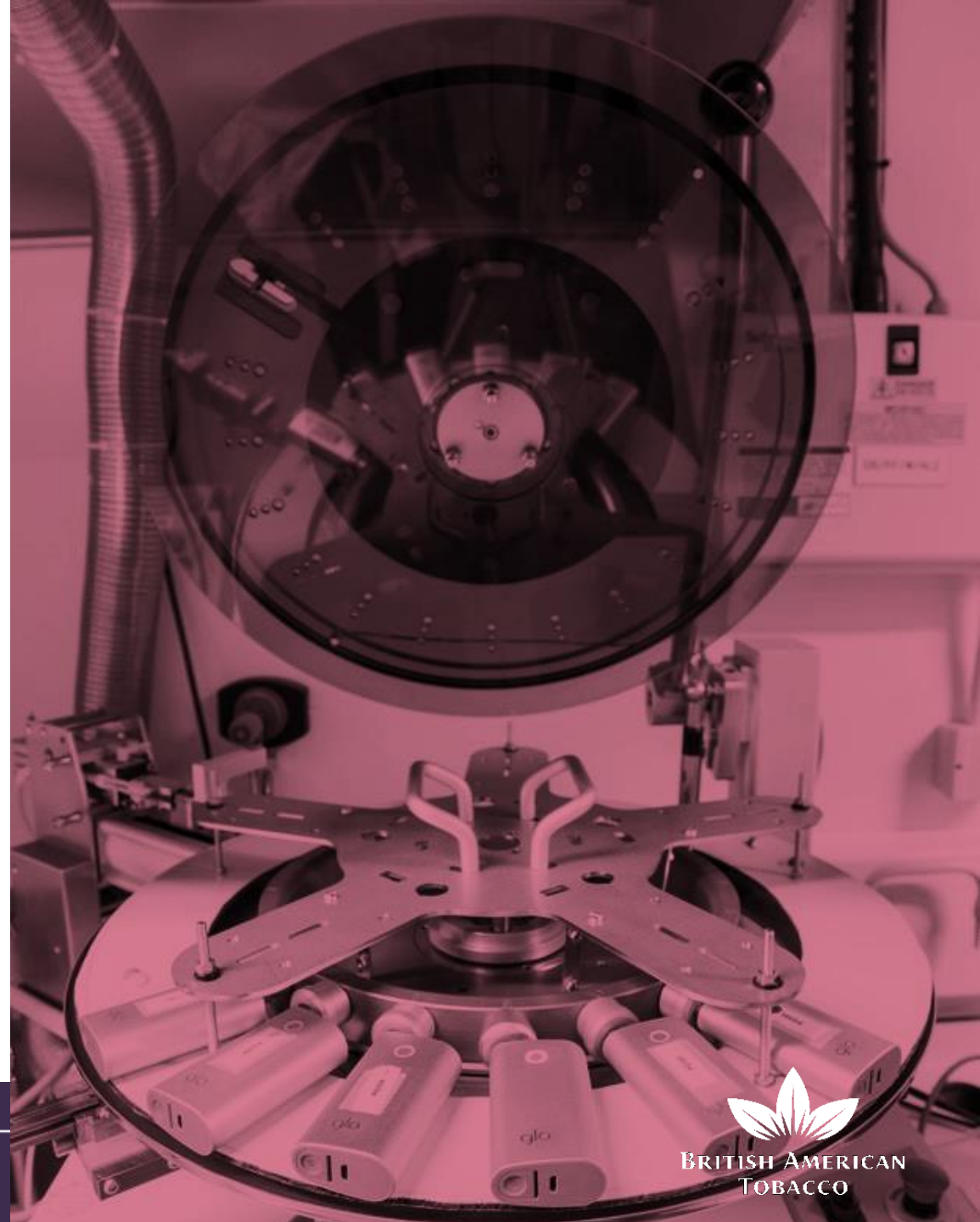
- **Data shows significant reduction in all BoEs** (with o-Tol sensitivity test) and in a number of cases these are similar reductions to nicotine cessation

- **These data may suggest the potential of glo THP as a potential reduced-risk product**

- **Further clinical studies would be necessary** to:

  -demonstrate that these reductions continue or are sustained

  -quantify any translation to reductions in smoking-related health risks i.e. Biomarkers of Potential Harm (BoPH)



Acknowledgement

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- Donald W. Graph
- Kirk Newland

- Mike McEwan
- Nathan Gale
- Alison Eldridge
- George Hardie
- Oscar M. Camacho
- John McAughey
- Chuan Liu
- James Murphy
- Chris Proctor

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- Max Scherer

THANK YOU

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