

A clinical study in Japanese smokers investigating changes in exposure to cigarette smoke chemicals in participants who switch to using a tobacco heating product for a five day period

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The glo™ Tobacco Heating Product

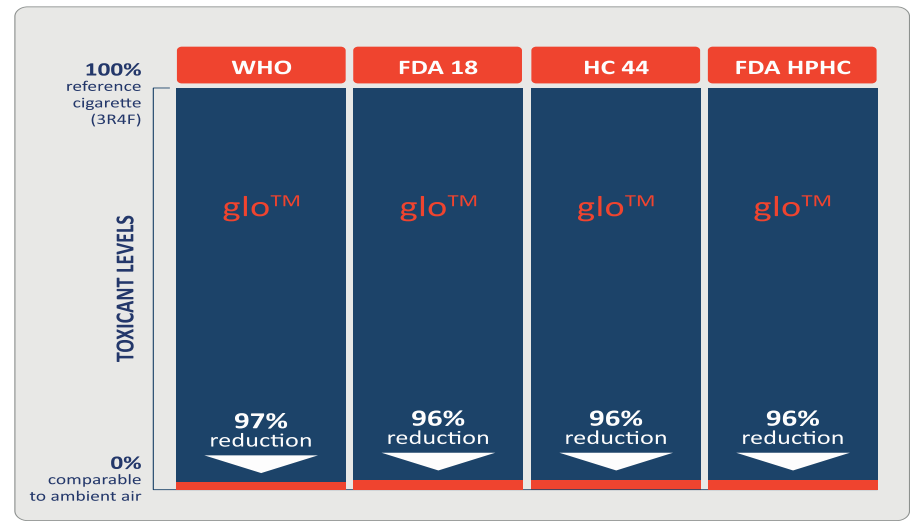


Battery-operated and recharged by microUSB

Heats a tobacco 'Neostik' to ~240°C

Neostiks are single-use and disposable

Emissions show much-reduced toxicant levels compared to cigarettes



Demonstrating Reduced Exposure – A BoE Study

- “A randomised, controlled, multi-centre open-label study in healthy Japanese subjects to evaluate the effect on biomarkers of exposure of switching from a conventional combustible cigarette to the glo™ tobacco heating product”
- ISRCTN14301360, UMIN000024988; IRB-approved



- Clinical conduct run at two clinics in Fukuoka, Japan




Objectives

Primary Objective


- To quantitatively assess within-arm changes in BoE and BoBE following a forced switch from a conventional cigarette to a NGP or cessation

Secondary Objectives

- To assess differences between arms in BoE and BoBE following a forced switch from a conventional cigarette to a NGP or cessation
 - To determine nicotine PK parameters for the study products
 - To assess subjects' satisfaction with the study products
 - To monitor the safety profile of subjects using THP products and conventional cigarettes, and subjects undergoing smoking cessation
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Study Population

- **Healthy male or female smokers, of Japanese origin, aged 23 – 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
 - **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

- **Biomarkers of Exposure (BoE)** to a range of particulate and vapour phase smoke constituents:

- Carbon monoxide in exhaled breath
- Urinary biomarkers:

Biomarker	Smoke Constituent
Total Nicotine equivalents (Nic + 5)	Nicotine
Total NNAL	NNK
Total NNN	NNN
3-HPMA	Acrolein
HMPMA	Crotonaldehyde
S-PMA	Benzene
MHBMA	1,3-Butadiene

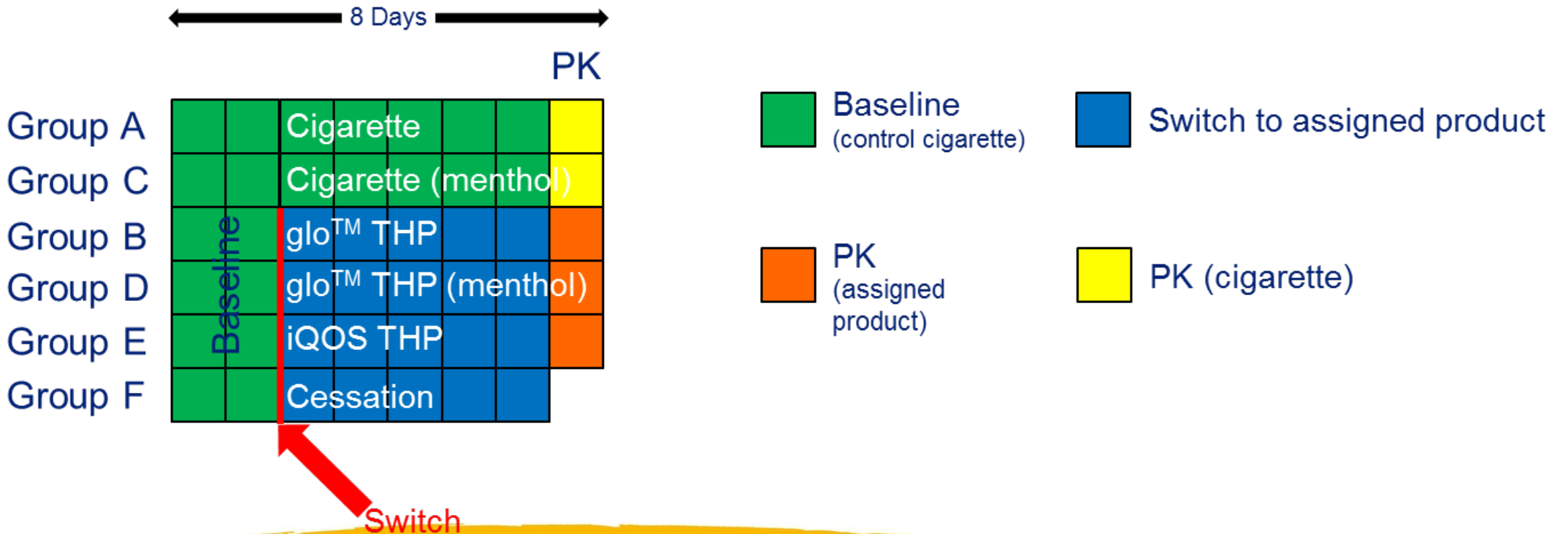
Biomarker	Smoke Constituent
CEMA	Acrylonitrile
4-ABP	4-Aminobiphenyl
o-Tol	o-Toluidine
2-AN	2-Aminonaphthalene
1-OHP	Pyrene
HEMA	Ethylene oxide
AAMA	Acrylamide
GAMA	Acrylamide

- **Additional endpoints**

- Biomarkers of effect - Urinary 8-epi-PGF₂α (Type III) and Blood white blood cell count
- Nicotine pharmacokinetics (C_{max} , T_{max} and AUC)

Study Design

- A multi-centre, randomised, open label, 6 arm, confinement study 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 = 180 subjects



Study Design

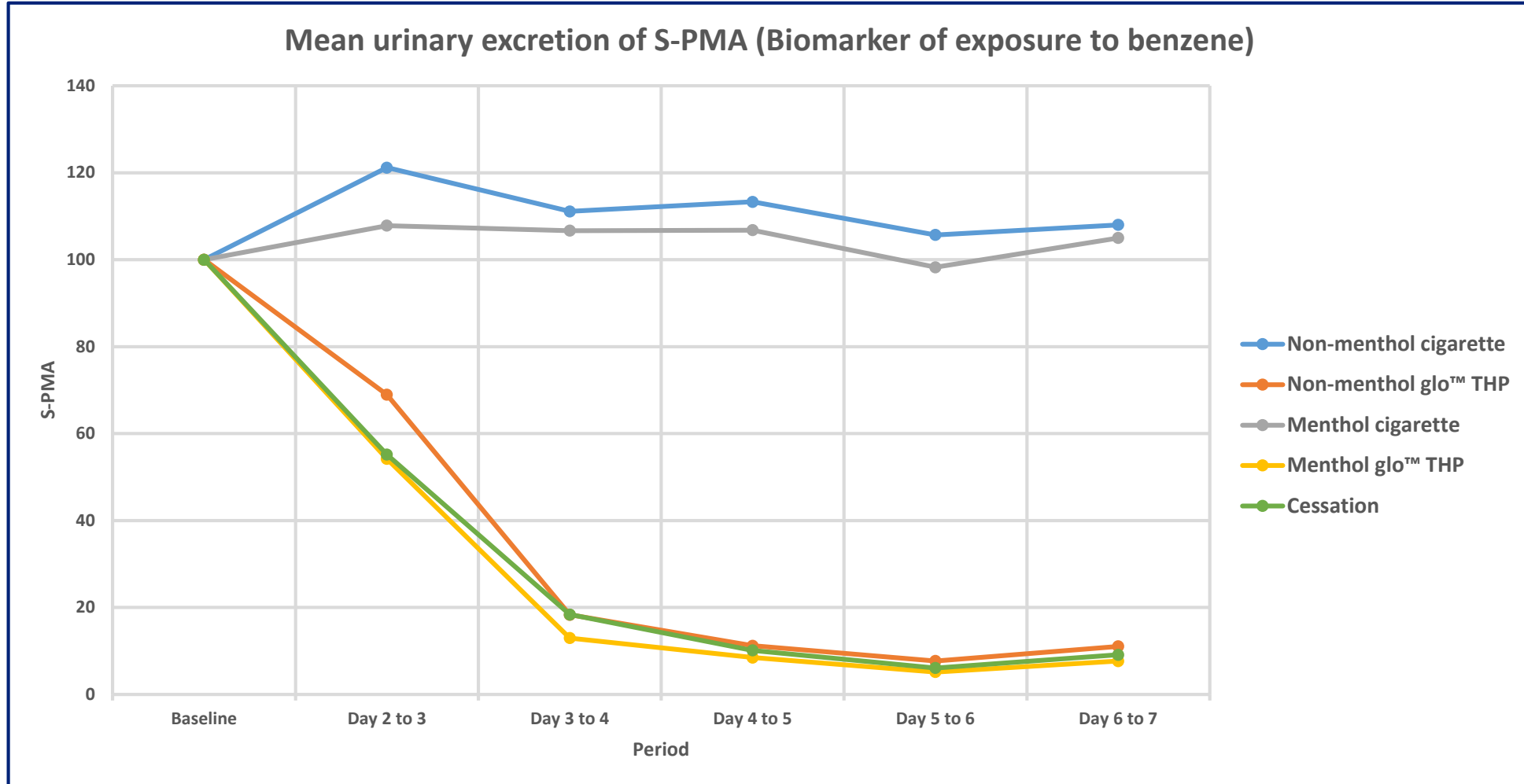
- *Ad libitum* use of all products in study (max. 120% of self-reported CPD)
 - Excluding cessation group from days 3 to 7
 - Menthol smokers were assigned to menthol products
- All urine voided by each subject collected over each 24-hour period (Days 1 to 7)
 - Urine tested for biomarkers of exposure
- Carbon monoxide in exhaled breath measured on all 7 days
- A 'spot' sample of blood also collected on Days 2, 5 and 7
 - Blood sample analysed for white blood cell count
- Nicotine pharmacokinetic assessment on Day 8 (excluding cessation group)
 - 12 hour nicotine abstinence
 - 5 minutes use of assigned product

Biomarkers of Exposure

- We have assessed the main biomarker of exposure data
 - Determined mean baseline excretion and mean excretion on each day, by group
 - N=30 for each group, unless stated otherwise
- In the subsequent line graphs, for clarity:
 - Data has been normalised (group mean baseline values set at 100)
 - Values above 100 indicate an increase in exposure
 - Values below 100 indicate a decrease in exposure
 - No variability estimates are shown
- We are yet to assess the biological effect markers and PK data

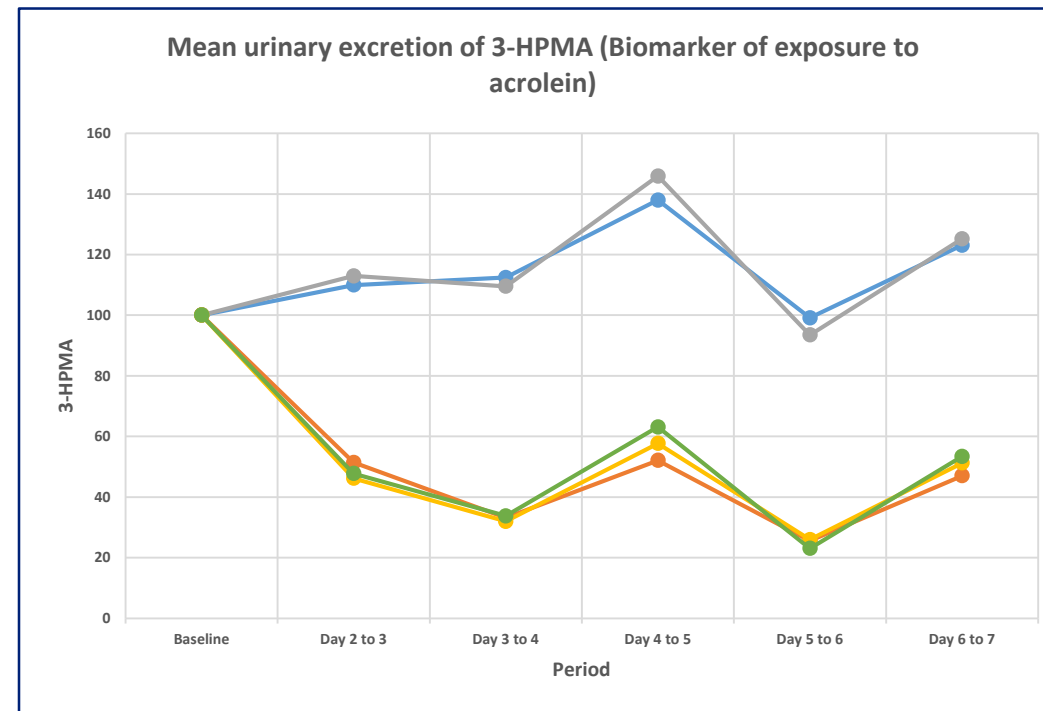
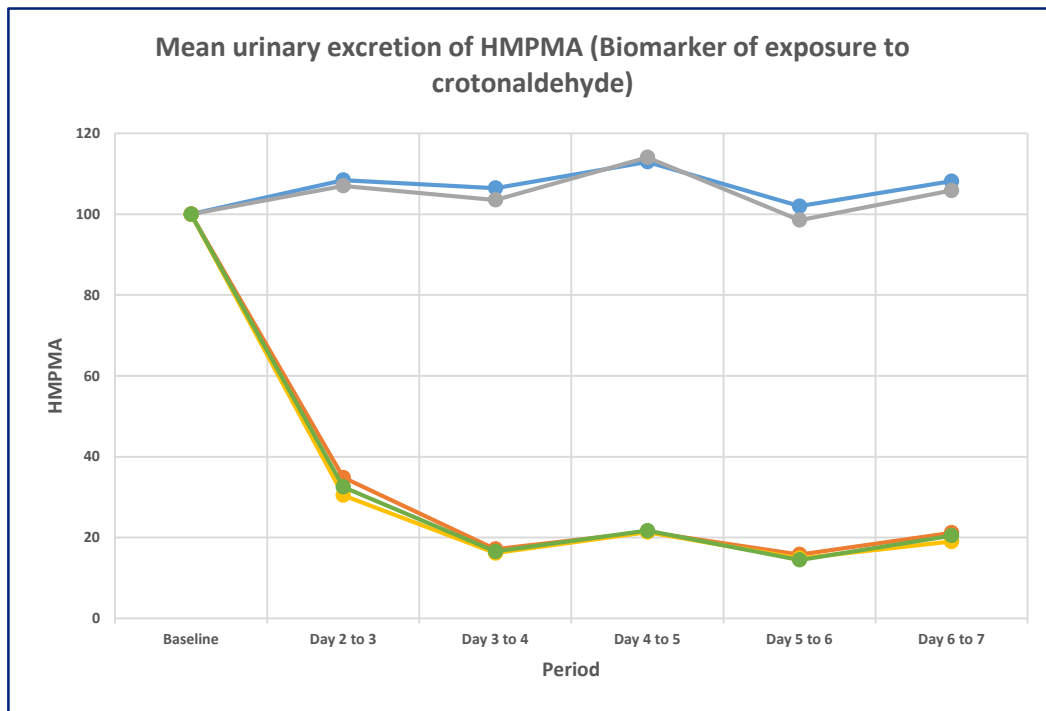
Biomarker of Exposure

To benzene



Biomarkers of Exposure

To other vapour phase toxicants

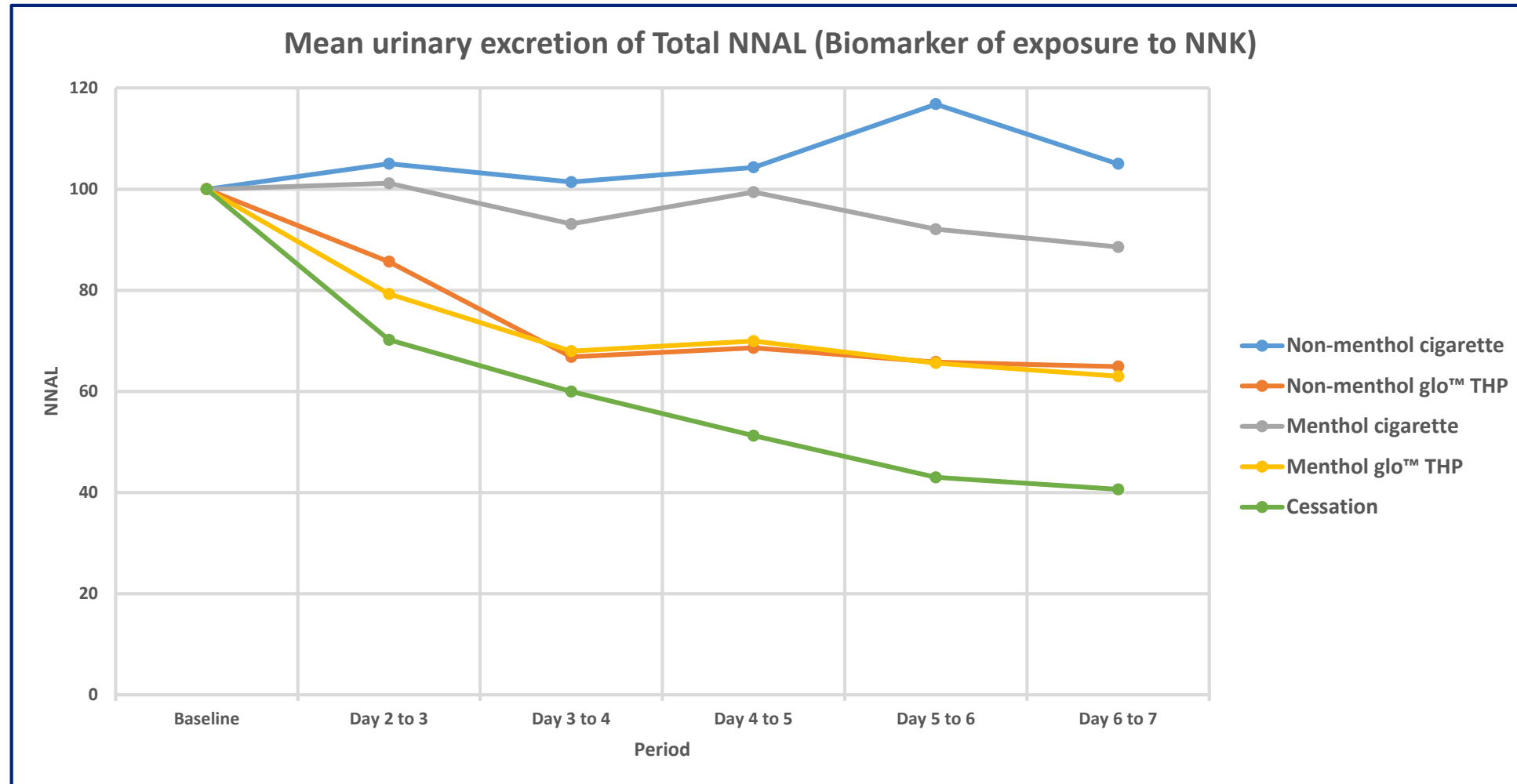


● Non-menthol cigarette
 ● Non-menthol glo™ THP
 ● Menthol cigarette
 ● Menthol glo™ THP
 ● Cessation



Biomarker of Exposure

To NNK

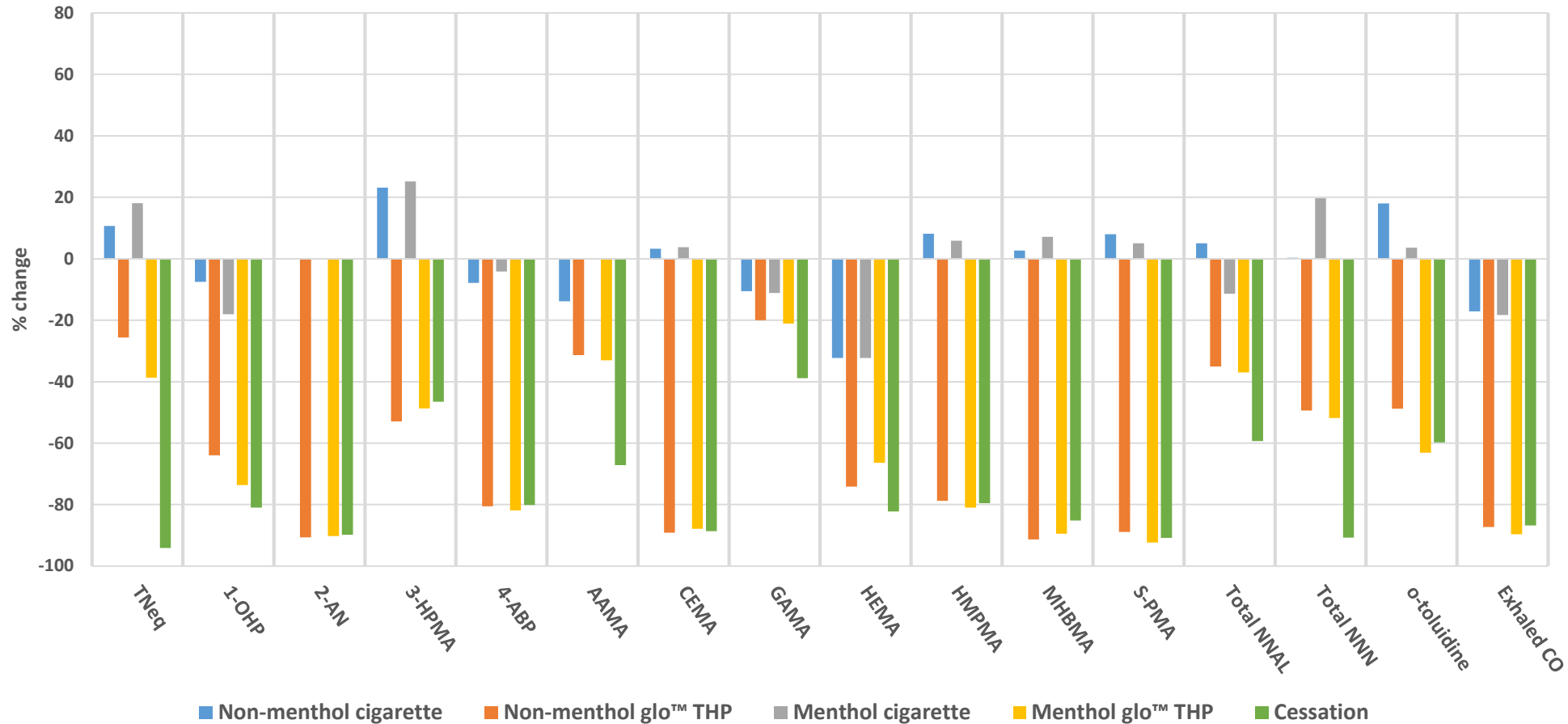




Biomarkers of Exposure

Summary

Mean excretion on Day 7 vs. mean excretion at Baseline



Summary

- First clinical study on the glo™ THP
- When smokers switched from smoking conventional cigarettes to glo™ THP, their exposure to cigarette smoke toxicants was significantly reduced
 - Variable reductions; many reaching levels similar to cessation
- These data may suggest the potential of the glo™ THP as a 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



Acknowledgements



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TOBACCO**



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