E-Cigarette Flavour Transfer Screening Method by GC/MS

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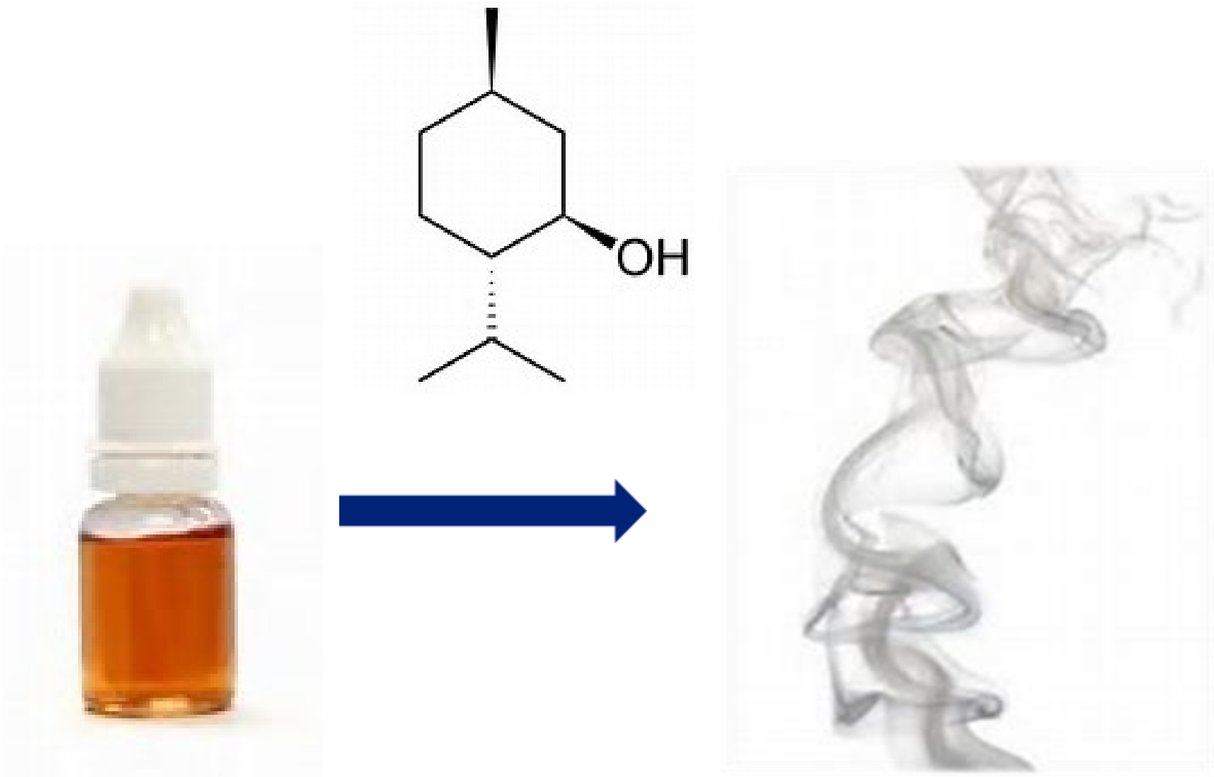
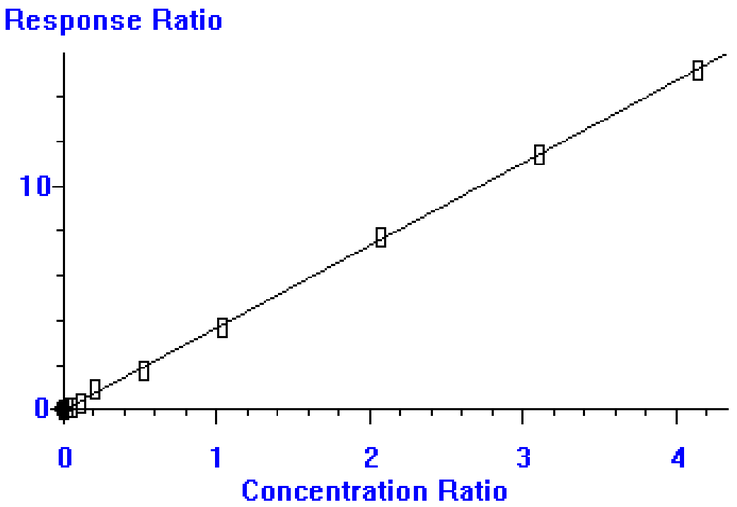
Introduction

- Importance of assessing flavour transfer
- Method overview
- Validation and results
- The Limit Test
- Summary & Conclusions
- Acknowledgements
- Questions



Importance of Assessing Flavour Transfer

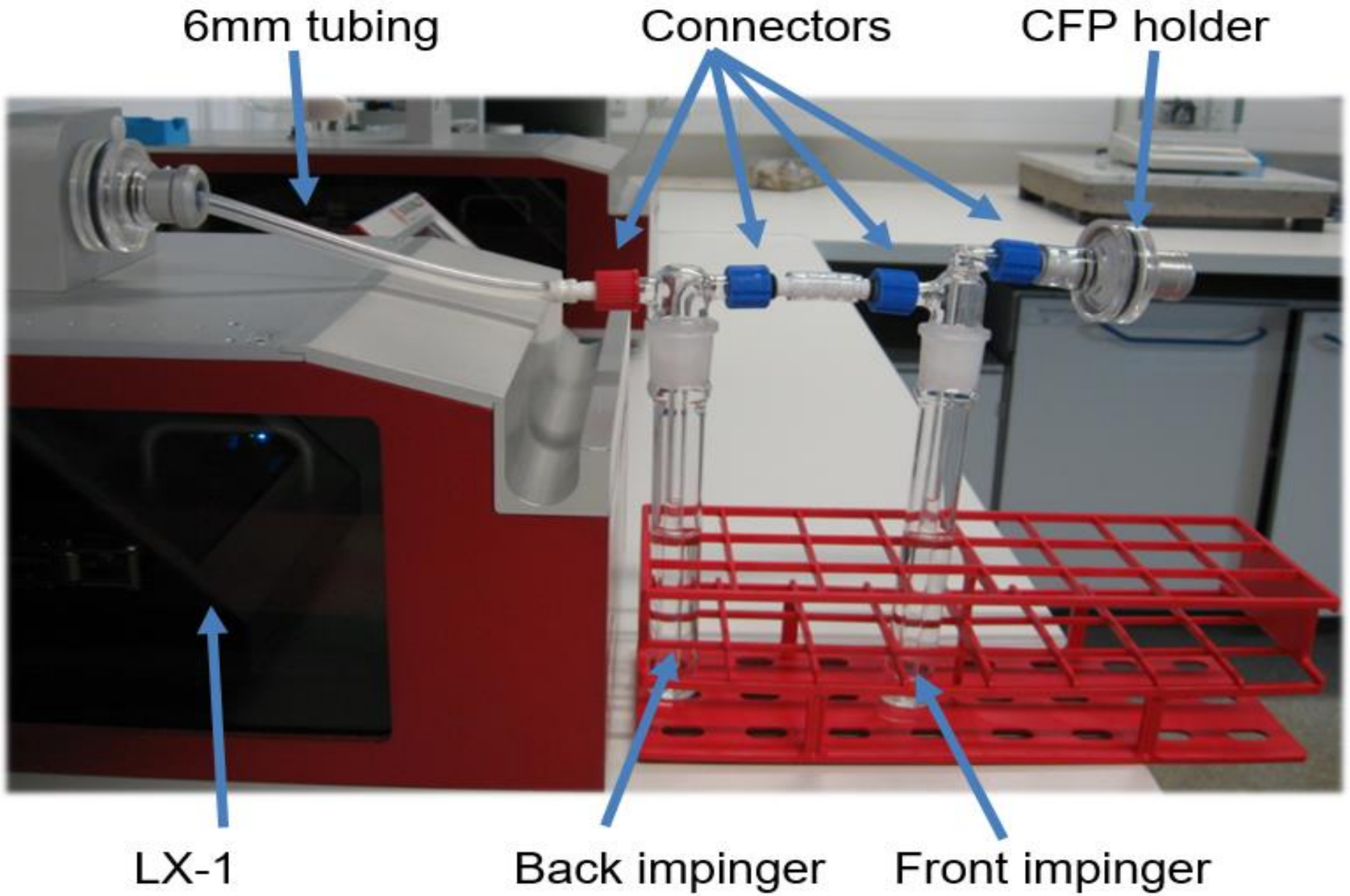
- Increasing requirement from a Stewardship perspective with regards to the transfer rate of certain flavour compounds from e-liquid to e-aerosol [1].
- Product development.
- Traditionally requires method development and validation of quantitative assays.



- The main objectives of this project were:
  - To provide a cost effective and fast turnaround (< 3 weeks) screening measurement for flavour transfer from e-liquids to e-aerosols.
  - To demonstrate whether transfer rates exceed BAT Stewardship Limits for defined compounds (Limit of Concern – LOC).
- The solution: a liquid to aerosol comparison method with Limit Test.

[1] Costigan, S. & Meredith, C: An approach to ingredient screening and toxicological risk assessment of flavours in e-liquids, Regulatory Toxicology and Pharmacology, Volume 72, Issue 2, July 2015, Pages 361-369.

Method Overview
Collecting the aerosol



- Extraction solution – ethanol containing internal standard (anisole-d8 @ 1µg/mL)
- 20mL / impinger
- All extractions use same batch of extraction solution
- 80mL puff volume, 3 sec puff duration, 30 sec puff interval

Method Overview

Generating the samples and calculating transfer

1) Collect emission on 44mm CFP + 2 impingers. Record device mass loss (DML - e.g. 500mg) n = 5

2) Recover condensed aerosol in holder using ¼ CFPs

3) Flush front impinger tubing and use to extract CFP + ¼ pads

4) Back impinger - vialled-up separately

5) Weigh & dilute with extraction solution equivalent e-liquid (500mg) n = 5

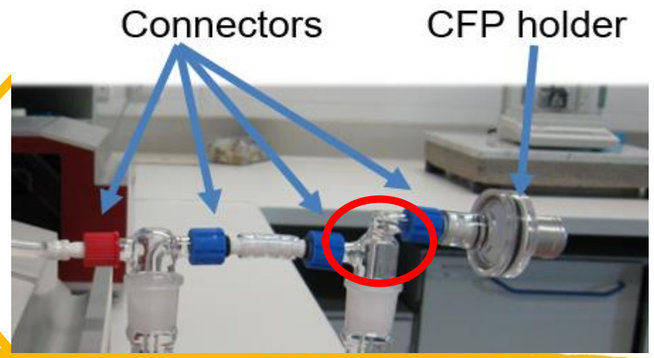
6) Analyse by Liq. Inj. GC/MS (SIM)

7) Calculate peak area ratios (PARs)

8) Normalise PARs to target DML (500mg)

9) Transfer rate (%) =

(total aerosol PAR / e-liquid PAR) x 100



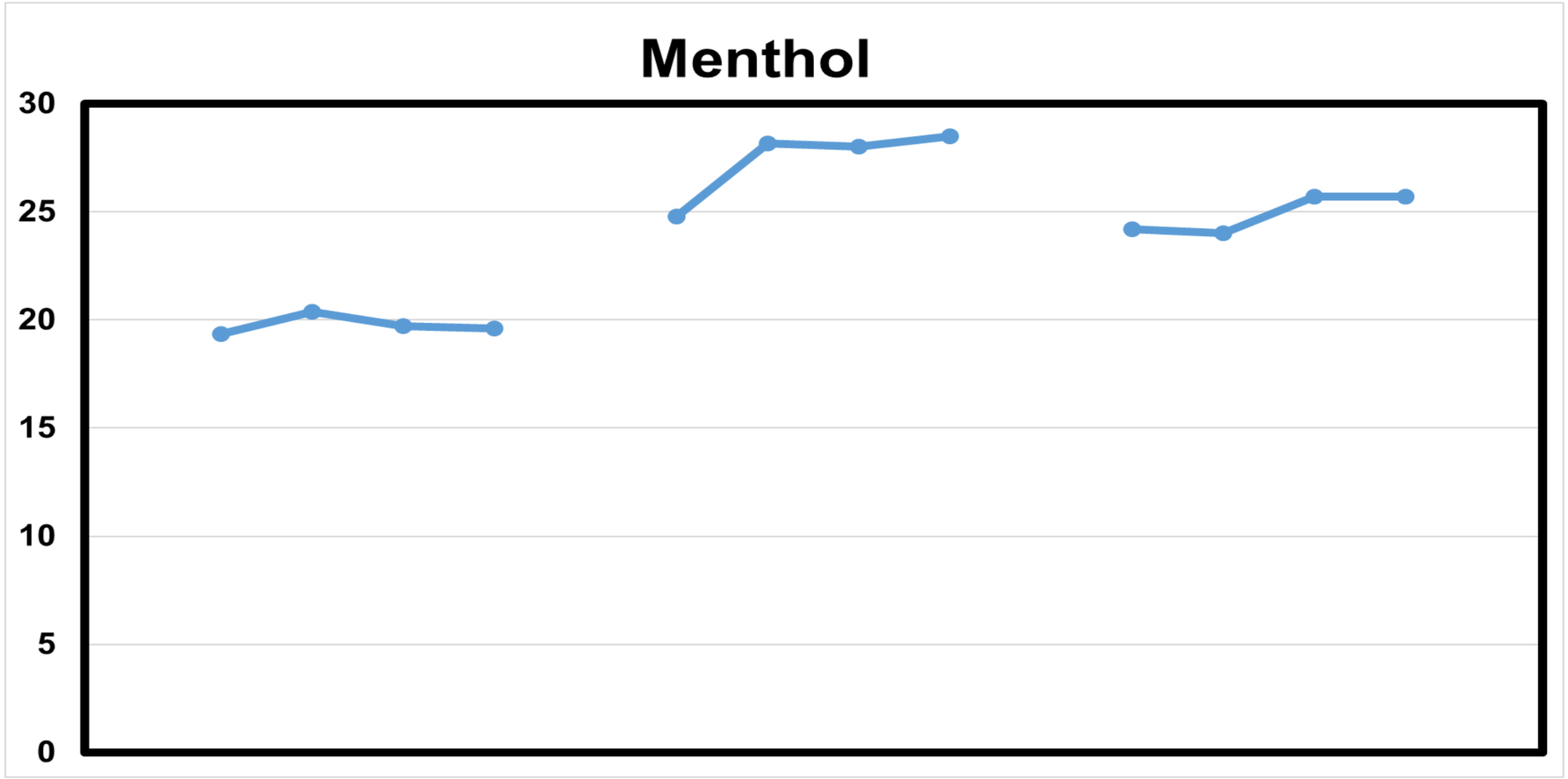
Validation and Results

- Target analytes: Limonene, Neomenthol, Menthol (peppermint oil e-liquid)

Criterion	n	Description
Extraction time optimisation	3	25 puffs 20mg/puff device (peppermint oil) onto CFP, extract in 20mL ethanol, aliquots taken 5, 10, 15, 20 minutes. Analyse in SCAN and SIM modes. Determine optimum extraction time.
Sintered vs Non-sintered impingers + distribution	5	Check for differences in trapping efficiency (e.g. more or less carry-over to 2nd impinger). Target ≤ 10% carry-over to back impinger.
Injection precision	5	Repeat injection of the same diluted e-liquid sample. Evaluate precision (≤ 1%).
Instrument carry-over	N/A	Instrument blanks analysed between samples, compound carry-over ≤ 1% assessed by peak area.
Method repeatability	5	RSD ≤15% for all analytes

Validation and Results
- Extraction time optimisation

- 15 minutes @ 180rpm selected as optimum extraction time



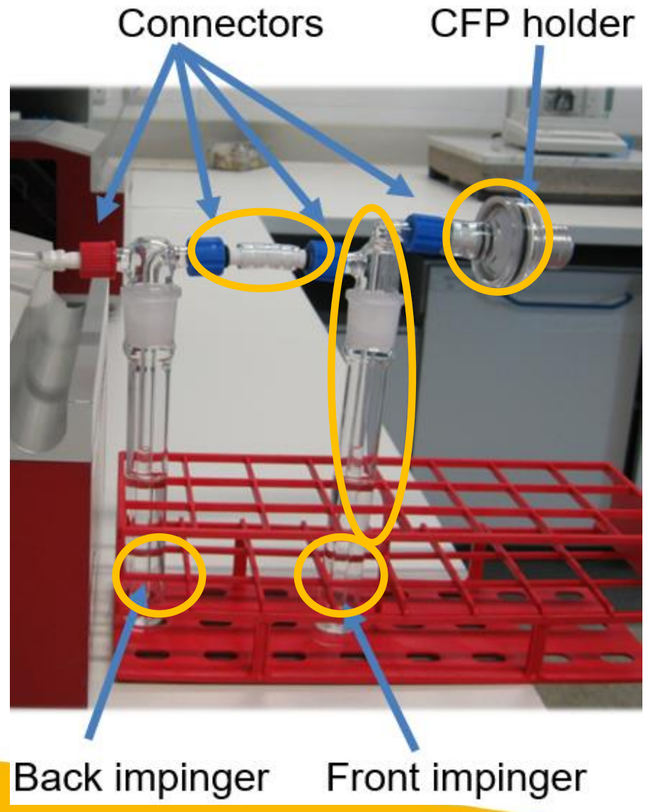
Extraction at 5/10/15/20 minutes (n = 3)

Validation and Results
- Analyte distribution

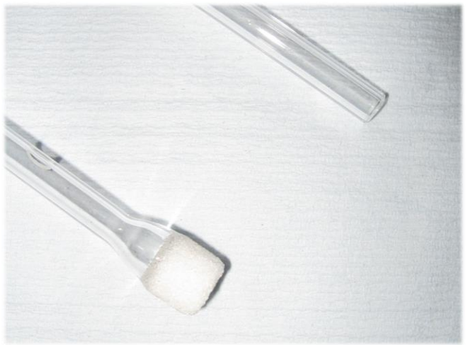
Sintered (%)	CFP	Down. Tube	Front Imp.	Bridge	Back Imp.
Limonene	2.4	3.9	93.0	<LOD	0.7
Neomenthol	87.8	0.8	11.4	<LOD	<LOD
Menthol	95.1	0.5	4.4	<LOD	<LOD

Non-Sintered (%)	Front Imp. + CFP	Back Imp.
Limonene	93.8	6.2
Neomenthol	98.9	1.1
Menthol	99.6	0.4

- Non-sintered - up to ~6% carry-over to back impingers.



Non-Sintered



Sintered

Validation and Results
- Assessing Transfer (n = 5)

Sintered Impingers	Mean Transfer (%)	SD Transfer	%RSD	U
Limonene	50	4	9	9
Neomenthol	87	5	6	10
Menthol	93	5	5	10

Non-Sintered Impingers	Mean Transfer (%)	SD Transfer	%RSD	U
Limonene	54	2	3	3
Neomenthol	92	2	2	4
Menthol	97	2	2	4

Quantitative Results	Mean Transfer (%)	SD Transfer	%RSD	U
Limonene	63	6	9	11
Neomenthol	82	1	2	2
Menthol	87	1	1	2

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Validation and Results
Sintered vs Non-Sintered vs Quantitative

- All methods show %RSD of ≤ 10% (n = 5).
- Comparable results to quantitative method.
- Non-sintered impingers showed up to 6% break-through to back impinger. However:
  - Non-sintered - Mean % transfers were higher.
  - Non-sintered - Best overall %RSDs.
  - Non-sintered - Much easier to clean!
- More variability associated with sintered impingers – this section is hand made.

Validation and Results
- Injection precision

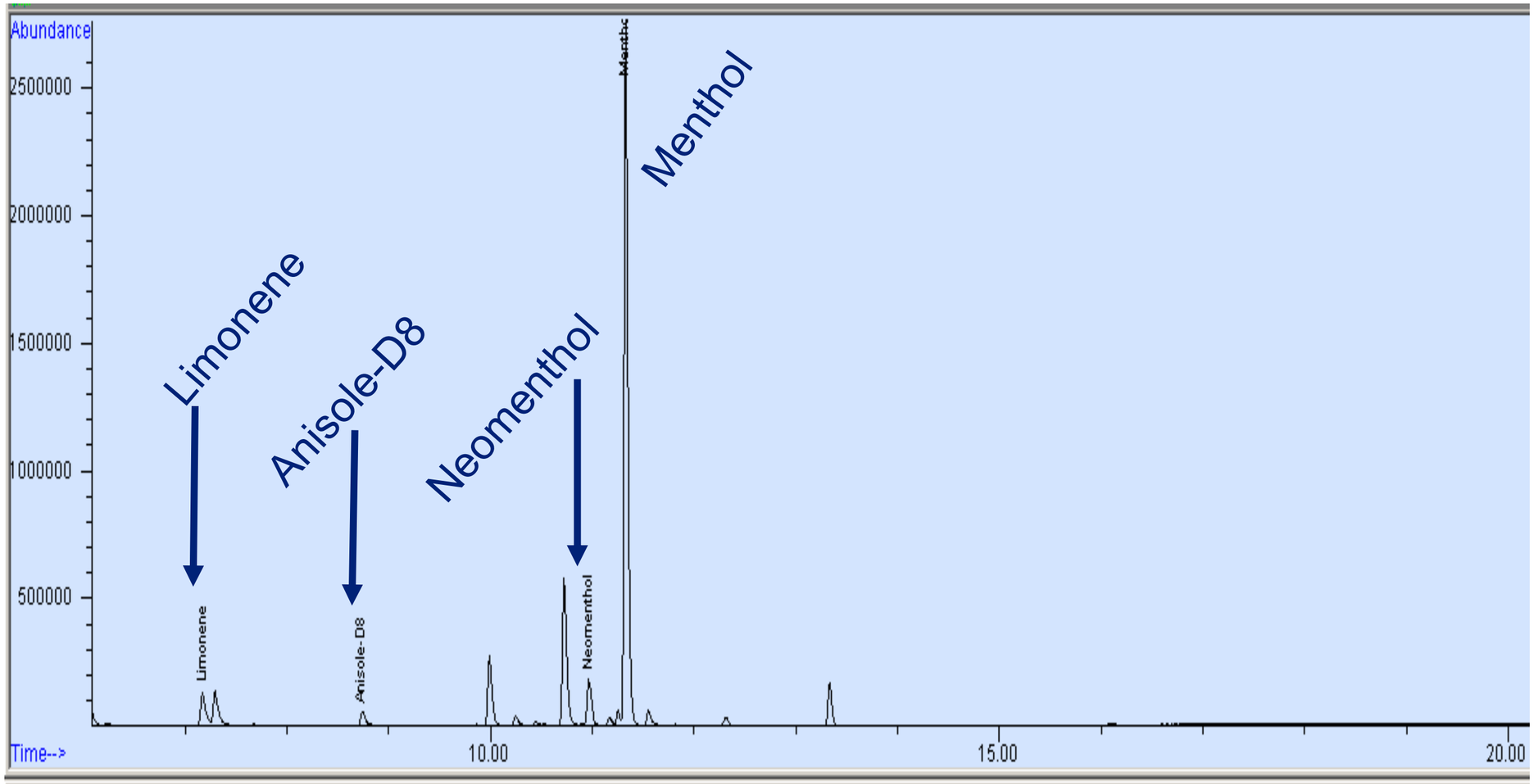
- Injection repeatability acceptable for both measured peak area and PAR.

Compound	Peak Area %RSD	PAR %RSD
Limonene	2.60	0.34
Neomenthol	2.08	1.30
Menthol	2.29	1.43
Anisole-D8 (Int. Std.)	2.48	N/A

- GC/MS sample carry-over in solvent blanks < 1% assessed by peak area.

Example Aerosol Chromatogram

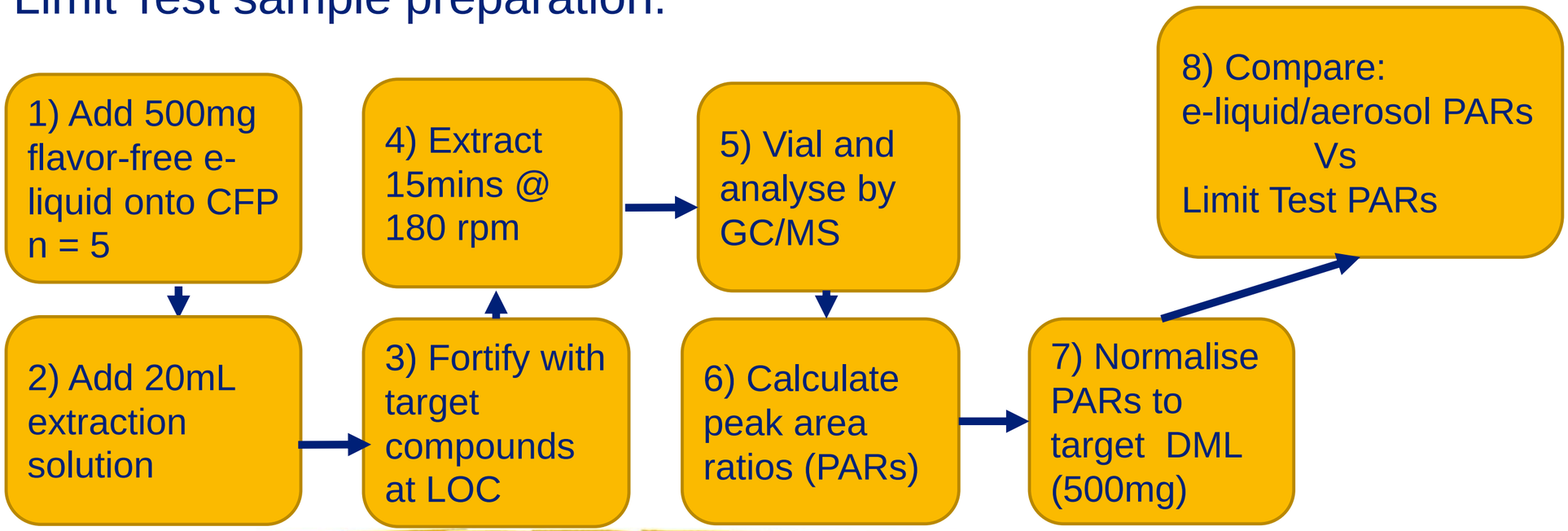
- Target compounds - selected ion monitoring (SIM)
- Stabilwax-DA: 30m x 0.25mm x 0.5µm GC column



The Limit Test

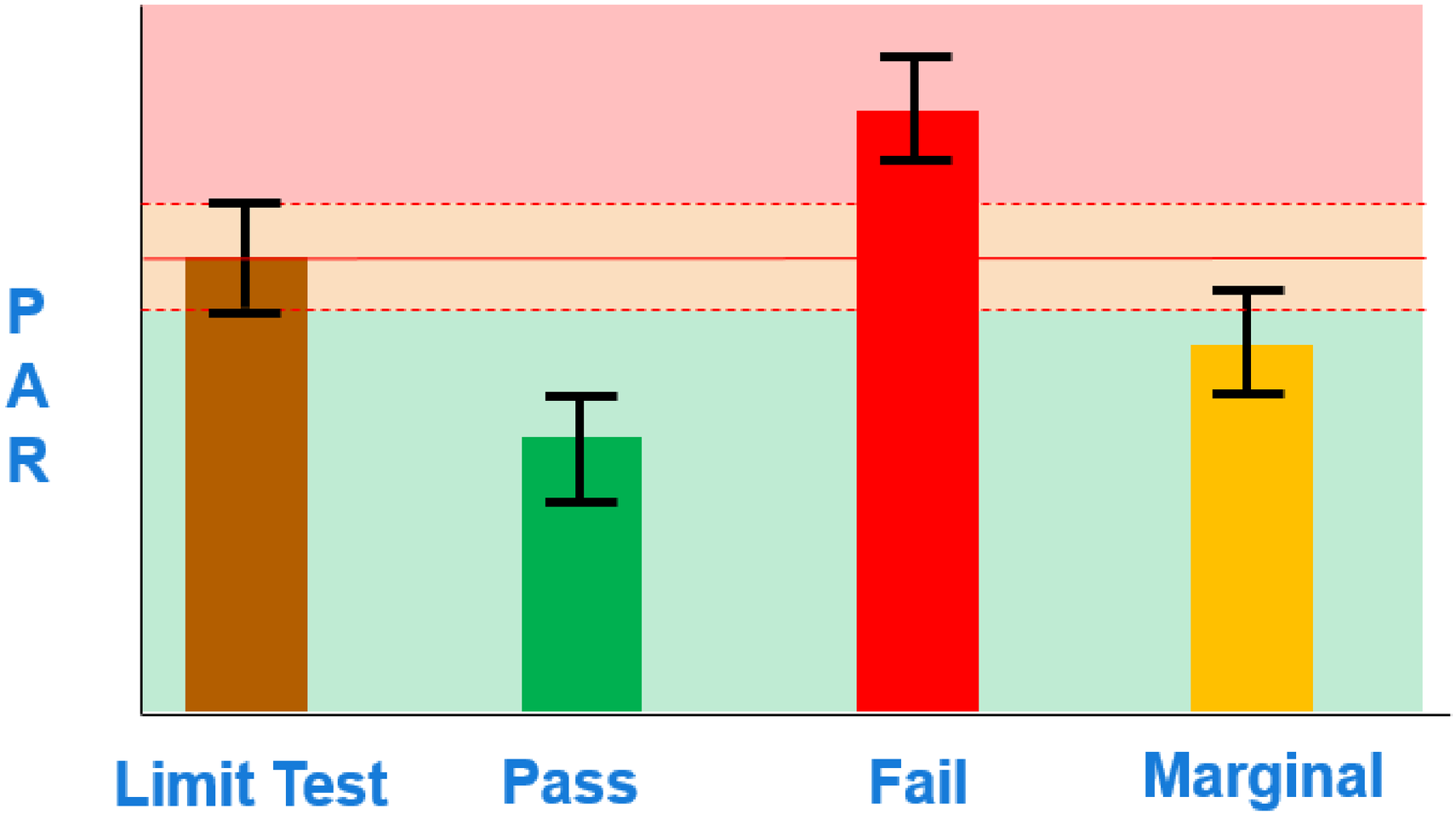
- Are target compounds above or below defined thresholds (Limit of Concern) taking into account the uncertainties?
- Samples prepared so far:
  - Aerosol impinger extracts (n = 5): 
  - E-Liquid extracts (n = 5): 

- Limit Test sample preparation:



The Limit Test
Red, Amber, Green (RAG)

- Possible outcomes:



Summary & Conclusions

- Presented a screening approach to flavour transfer:
  - CFP & liquid impingers
  - Use of peak area ratios for relative rather than absolute measurement of transfer

- Discussed concept of Limit Test:
  - RAG approach
  - Fail/succeed, fast/cheap

- The end of the calibration curve?
  - NO!

- Approach may also be applicable to tobacco heating products (THPs) and combustibles.

Acknowledgements and Reference

- Colleagues at BAT Analytical Development Centre

Stuart Martin  Malcolm Saxton  Louise Bishop 

- Reference:

[1] Costigan, S. & Meredith, C: An approach to ingredient screening and toxicological risk assessment of flavours in e-liquids, Regulatory Toxicology and Pharmacology, Volume 72, Issue 2, July 2015, Pages 361-369.

Thank you for listening, any questions?

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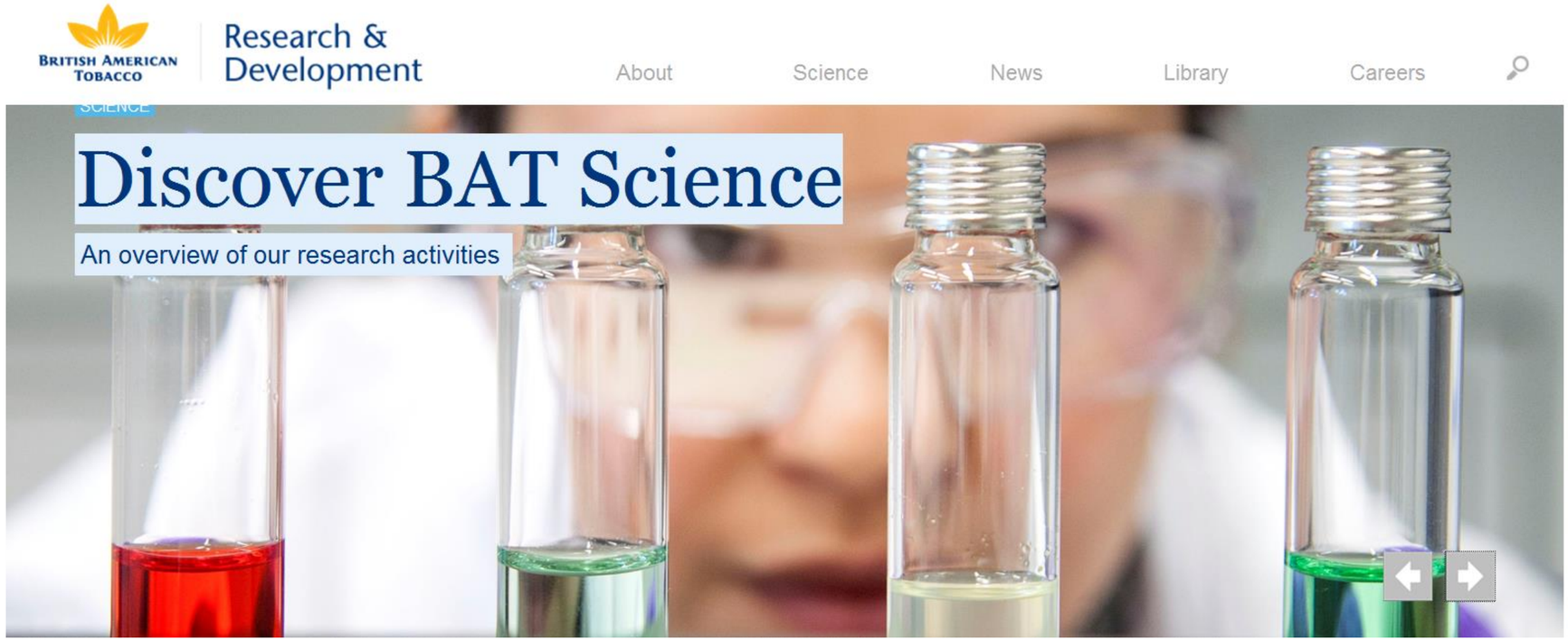

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