A Framework for the Systematic Evaluation of a Novel Cigarette Filter Technology

David Thorne, David Waters,[1] Ian Crooks,[1] Mark West,[1] Krishna Prasad,[1] Adam Gray,[1] Casandra West,[2] Peter Wan,[1] Richard Savory,[1] Ignacio Suarez,[1] Carolina Garcia-Canton[1]

[1]B.A.T. (Investments) Limited, Regents Park Road, Southampton, Hampshire, SO15 8TL, UK
[2]RAI Services Company, 950 Reynolds Blvd. Winston-Salem, NC 27105, USA

Correspondence: David_Thorne@BAT.com

CORESTA CONGRESS 2024
STPOST47

Introduction

Any functional change to cigarette filter design warrants a rigorous assessment to ensure comparability to existing filter functionality. This study compared the functionality of a novel cellulose-based alternative with a standard cellulose acetate (CA) filter using a combination of emissions, *in silico* approaches, *in vitro* assessments, and behavioural studies. The aim of the study was to establish a weight of evidence assessment framework for the comprehensive evaluation of a novel cigarette filter design to support a robust stewardship approach. The data showed the novel cellulose-based alternative to be comparable to a standard CA filter across all assessments. The study utalises a comprehensive step-wise assessment framework for future use to identify potential increases in toxicant emissions and exposures associated with using a novel filter technology.

Methodology

Study design: The approach assessed changes in the resulting cigarette smoke under both ISO and HCI smoking regimes to ensure emission profiles between the novel and conventional filters remained comparable. An *in silico* desk based risk assessment, and a full *in vitro* toxicology package helped demonstrate functional equivalence between the two technologies. Finally, behavioural aspects were assessed, to ensure smoking behaviour was not adversely affected by filter technology change.

Test products: Three prototype cigarettes were manufactured for the investigation. They shared the same conventional tobacco blend. The control cigarette had a standard CA filter. The test cigarette had the novel cellulose-based filter technology. The third cigarette was unfiltered. 3R4F Kentucky reference cigarettes were included in the smoke chemistry and *in vitro* analyses, for comparison with historical results and to provide context.

Smoke chemistry: A full Hoffmann mainstream cigarette smoke assessment was conducted under ISO and HCI conditions at Labstat International ULC (Kitchener, Ontario, Canada). **Table 1.**

In silico: Excessive lifetime cancer risk (ELCR) and Hazard Index (HI) were modelled with and without phenols and cresols to establish a point of comparison. **Table 2.**

In vitro [1-3]**:** Total particulate matter (TPM) was generated by smoking cigarettes on a Borgwaldt RM200s smoking machine under the ISO regimen, approximately 150 mg TPM per 44 mm Cambridge filter pad was collected. TPM was used in all *in vitro* assays: Neutral Red uptake assay (NRU), Bacterial reverse mutation (Ames) test, Mouse lymphoma assay (MLA), and *In vitro* micronucleus (IVMN) Test. **Figures 1-3.**

Behavioural studies: Puffing topography and mouth level exposure (MLE) per cigarette, via optical obscuration, were measured with 65 subjects. The average daily consumption (ADC) and MLE (per cigarette and per day) via part-filter method were measured in 67 subjects. **Table 4**.

References

1. OECD Guideline No. 432: In Vitro 3T3 Phototoxicity Test.
2. OECD Guideline No. 471: Bacterial Reverse Mutation NRU Test.
3. OECD Guideline No. 487: In Vitro Mammalian Cell Micronucleus Test.
4. Eldridge et al., 2015. Variation in tobacco and mainstream smoke toxicant yields from selected commercial cigarette products. Reg Tox Pharm. 71, 3 409-427.
5. Jackson et al., 2016. Mouth Level Exposure and Similarity to Machine-smoked Constituent Yields. Tob Regul Science 1, 2 (1) 3-8.

Results

Smoke chemistry: Emissions analysis showed variations in the chemical profile for the cellulose-based alternative filter when compared to the standard CA control. However, the observed variation was within the 95th % for a global FMC 7 mg product for most Hoffmann analytes[4]. Those exceeding are detailed below.

Analyte	ISO		HCI	
	CA	Cellulose-based alternative	CA	Cellulose-based alternative
CO (mg/cig)	6.56 ± 0.37	**9.27 ± 1.02**	20.6 ± 0.98	**25.58 ± 1.18**
Phenol (µg/cig)	11.3 ± 0.92	**24.38 ± 1.18**	21.93 ± 1.95	**84.9 ± 12.71**
Pyridine (µg/cig)	6.57 ± 0.83	**14.7 ± 2.33**	28.98 ± 4.5	**47.61 ± 6.12**
m-Cresol (µg/cig)	2.22 ± 0.11	**3.48 ± 0.2**	4.09 ± 0.44	**11.61 ± 1.7**
o-Cresol (µg/cig)	2.88 ± 0.23	**4.97 ± 0.27**	4.93 ± 0.44	**16.6 ± 2.53**
p-Cresol (µg/cig)	5.55 ± 0.29	**9.27 ± 0.3**	10.37 ± 1.18	**31.53 ± 4.57**

CA = cellulose acetate control.
Statistically significant increases, compared to the controls in **bold** respectively.

Table 1. Shows those analytes that were outside of the 95th % for a global FMC 7 mg product, under both smoking conditions.

***In silico*:** ELCRs and HIs were calculated for each product under both HCI and ISO smoking regimes separately. Compared to the CA, the novel filter had no effect on HI (non-cancer) and no effect ELCR (cancer) within a population based on modelling approach. All values were within the ranges expected for combustible cigarettes and no difference was observed for phenolic changes in the novel filter compared to CA.

10 cigarettes per day					
HI					
Disease	CA	Cellulose-based	CA[a]	Cellulose-based[a]	Range[b]
Respiratory	3000	3000	3000	3000	4000-5000
Cardiovascular	3000	3000	3000	3000	4000-5000
Reprodev	30	30	30	30	20-30
Total	3000	3000	3000	3000	4000-5000
ELCR					
Cancer	4E-03	4E-03	4E-03	4E-03	5-6E-03
20 cigarettes per day					
HI					
Respiratory	6000	6000	6000	6000	8000-10000
Cardiovascular	6000	6000	6000	6000	8000-10000
Reprodev	50	50	50	50	40-60
Total	6000	6000	6000	6000	8000-10000
ELCR					
Cancer	7E-03	8E-03	7E-03	8E-03	9-10E-03
30 cigarettes per day					
HI					
Respiratory	9000	9000	9000	9000	10000-20000
Cardiovascular	8000	9000	8000	9000	10000-10000
Reprodev	80	80	80	80	70-90
Total	9000	9000	9000	9000	10000-20000
ELCR					
Cancer	1E-02	1E-02	1E-02	1E-02	1-2E-02

[a] Including phenol (HI) and mixed cresols (ELCR).
[b] Without phenol and mixed cresols.

Table 2. Shows HI and ELCR results for HCI smoking only. Jackson et al. (2016)[5] suggested that HCI machine smoked values may be more representative of smokers' exposure compared to that of ISO. Regardless of regimen assessed, the values for either HCI or ISO did not exceed that of the range for other similar commercially available cigarettes, although variations between the novel cellulose-based and CA were observed depending on regimen.

In vitro: genetic tox analysis showed comparability between CA and a novel filter substrate for all assays and treatment conditions **(Figure 3, 4 and 5).** A 1R6F reference product was used to benchmark responses. All responses were comparable to this global reference and to the CA control, suggesting no additional risk for the novel filter over the CA.

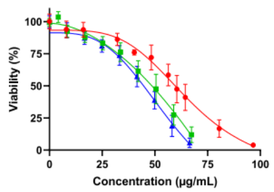

Figure 1. Shows the cytotoxic response of TPM generated from **3R4F**, **CA**, **Novel filter,** respectively.

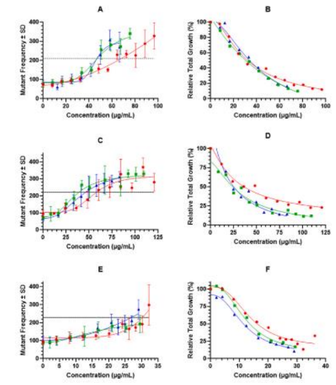

Figure 2. Shows mutation frequencies of TPM generated from **3R4F**, **CA**, **Novel filter,** respectively.

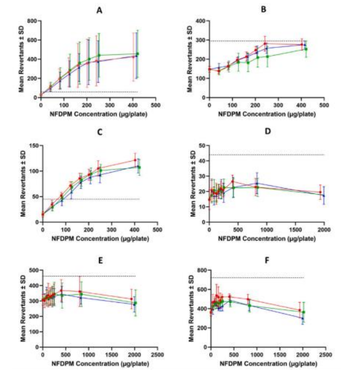

Figure 3. Shows bacterial mutations in TA98 and TA10 in the presence of S9 from TPM generated from **3R4F**, **CA**, **Novel filter,** respectively.

Behavioural studies: There were no significant differences observed between the standard CA and cellulose-based alternative in any of the puffing topography attributes, or MLE to NFDPM (mg/cig). MLE to nicotine was significantly lower in the novel technology compared to the standard CA (0.66 vs 0.91 mg/cig, p < 0.0001).

Puffing topography			
Attribute	CA (n = 65)[a]	Cellulose-based alternative (n = 65)[a]	p-value[b]
Puff count	11.2 ± 8.2	10.2 ± 6.9	0.0815
Puff volume (mL)	55.9 ± 19.3	55.7 ± 19.7	0.8953
Puff Duration (s)	1.65 ± 0.96	1.72 ± 0.90	0.3235
Interpuff interval (s)	11.0 ± 9.0	9.3 ± 7.8	0.1622
Session time (s)	103.9 ± 63.4	86.3 ± 54.9	0.0642
Pressure Drop (cm WG)	17.0 ± 5.4	16.3 ± 4.7	0.2263
Effort (cm WG s)	260.2 ± 160.0	237.2 ± 125.3	0.0787
MLE measurements			
MLE to NFDPM (mg/cig)	10.1 ± 6.9	9.4 ± 6.4	0.2919
MLE to nicotine (mg/cig)	0.91 ± 0.52	0.66 ± 0.42	<0.0001

b-Determined using paired *t*-test at 5% significance level (α). P-values <0.05 indicate a significant difference between products.
[a] 2 measures per subject (averaged).

Table 4. No significant differences observed in ADC or NFDPM per cigarette, however MLE to nicotine (per cigarette and per day) were significantly lower for the novel cellulose-based alternative compared to a CA filter.

Conclusion

In conclusion, using a systematic step-wise framework, we have comprehensively investigated multiple aspects of changing a standard cigarette filter design and shown comparability between the two technologies using a weight of evidence approach. Finally, and equally importantly, we have detailed the challenges of substituting a filter technology and the steps required to substantiate the change without a full product re-design.

Disclaimer:- Nothing in this study evaluated whether the experimental technology is at this time commercially feasible, scalable, or acceptable to consumers.

Follow us: www.bat-science.com welcometobat @BAT_Sci