THS 2.2 DORADO-II RON HPHCs COMPARISON TO COMBUSTIBLE REFERENCE PRODUCT 3R4F ANALYZED BY LABSTAT UCL

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1 Executive Summary

The present study compares the composition of the aerosol of a heated tobacco product (THS 2.2) to the composition of the smoke of a reference combustible cigarette (3R4F) based on the measurement of the PMI-58, our internal list of constituents we have established to compare the performance of heated tobacco products vs. combustible cigarettes. The PMI 58 list includes Harmful and Potentially Harmful Constituents (HPHCs) established by competent health authorities, such as the FDA 18, Health Canada (44) and WHO (39).

Based on the levels measured in THS 2.2 and 3R4F, we can calculate an average reduction of HPHCs of more than 92 % and 89 % on a stick basis or nicotine basis respectively for the THS 2.2 compared to the 3R4F.

The analytical work was performed by Labstat UCL, an independent laboratory.

2 Abbreviations

Abbreviation/Term	Explanation
EDMS	Electronic Document Management System
HPHC	Harmful and Potentially Harmful Constituent
ISO	International Organization for Standardization
LOQ	Limit of Quantification
µg	Microgram
MEK	Methyl Ethyl Ketone
mg	Milligram
NAB	N'-nitrosoanabasine
NAT	N'-nitrosoanatabine
ng	Nanogram
NNK	4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone
NNN	N'-Nitrosonornicotine

Abbreviation/Term	Explanation
NO	Nitric Oxide
NOx	Nitrogen Oxides
PAH	Polycyclic Aromatic Hydrocarbon
PMI	Philip Morris International
SD	Standard Deviation
Stk	Stick
TC	Training Center
THS	Tobacco Heating System
TPM	Total Particulate Matter
TSNA	Tobacco-Specific Nitrosamine

For complete definition, refer to PMI OPS Glossary and PMI RD Glossary.

3 Purpose

The present study compares the aerosol composition of a heated tobacco product (THS 2.2) to the composition of the smoke of a reference combustible cigarette (3R4F) based on the measurement of the PMI-58, our internal list of constituents we have established to compare the performance of heated tobacco products vs. combustible cigarettes. The PMI 58 list includes Harmful and Potentially Harmful Constituents (HPHCs) established by competent health authorities, such as the FDA 18, Health Canada (44) and WHO (39).

The present study report focuses on the calculation of reduction of HPHCs between the aerosol of the THS 2.2 against the smoke of a reference conventional cigarette (3R4F), based on analytical data measured by an independent Laboratory, Labstat UCL.

4 Research Question

The goal of the study is demonstrate HPHCs reduction of THS 2.2 heated tobacco product against combustible product using 3R4F as a reference cigarette.

The analyses have performed according to testing protocol P1_THS 2.2_EXPT004923_Testing Protocol for Regulatory submission [1] and related testing order (TO): TO-10855

5 Methods

The detail of the analytical methodology is report in the Labstat report [2] NS308-H.

6 Results

6.1 Data availability

Data considered in the present report were obtained and reported by Labstat International ULC. Labstat International ULC warrants that all sample(s) were tested in accordance with its standard test procedures and in accordance with its ISO 17025 accreditation.

Table 1: Data considered in the present report.

Product Description	*Labstat Codes*	*Sample numbers*	*Replicates per HPHC*
Batch of SMS.002569.RD(1) Platform 1 ZRH/THD 2.4/ZRH holder firmware - 1.1.1 (v2.4)/C28/FPD 4.4 Tobacco Stick Holder (THD v2.4) - beta Dark Slate - Platform 1 – ZRH / C3.2 / Dorado II / CL / Flavor AC Ron regular composite batch	1680386	SMP060595	3 replicates per sample

6.2 Results Dorado-II Ron

Summary statistics and Table 3. Average reduction on stick basis and on nicotine basis are calculated from Table 3 to exclude the main aerosol deliveries (TPM, nicotine, glycerine and water) from the reduction.

Table 2: Main aerosol deliveries

Aerosol deliveries according to ISO 4387; 8454; 1035	Unit	3R4F			THS 2.2		
		mean	SD	n	mean	SD	n
Glycerol[1]	mg/stk	2.08	0.113	2	5.02	0.101	3
Nicotine	mg/stk	1.74	0.039	2	1.29	0.047	3
Nicotine Free Dry Particulate Matter (NFDPM)[2]	mg/stk	25.0	1.14	2	19.4	1.62	3
Total Particulate Matter (TPM)	mg/stk	41.4	3.28	2	50.9	2.90	3
Water[2]	mg/stk	14.7	2.10	2	30.2	2.17	3

[1] *product specific not part of ISO parameter*

[2] *Due to the high water content of the THS 2.2 aerosol, accurate water measurements cannot be obtained with the ISO standard methods. ISO parameters based on water measurements conducted according to ISO standard cannot be considered and in addition they do not account for aerosol formers such as glycerol which constitute a major part of the THS 2.2 aerosol. For this reason the use of terms NFDPM to describe the aerosol collected mass from THS 2.2 may be misleading given the very different constituent make-up in comparison to conventional products. Alternatively accurate water measurements in the THS 2.2 aerosol require the establishment of new analytical methods. Read more in Ghosh, D. & Jeannet, C. (2014). An Improved Cambridge Filter Pad Extraction Methodology to Obtain More Accurate Water and "Tar" Values: In Situ Cambridge Filter Pad Extraction Methodology. Beiträge zur Tabakforschung / Contributions to Tobacco Research, 26(2), pp. 38-49*

Table 3: HPCHs from the PMI-58 (excluding main aerosol deliveries reported in Table 2) When results were either below the LOQ or the LOD, results are shown with " < value of LOQ/LOD", and the % of reduction vs. 3R4F was calculated using the LOQ or LOD value respectively for the THS. When both the THS and the 3R4F were below the LOQ/LOD, no reduction can be calculated.

HPHCs (alphabetic order)	Unit	3R4F			THS 2.2			% on stick basis		% on nicotine basis	
		mean	SD	n	mean	SD	n	% of 3R4F	% of reduction to 3R4F	% of 3R4F	% of reduction to 3R4F
1,3-Butadiene	µg/stk	89.2	1.73	2	0.207	0.0160	3	0.2%	99.8%	0.3%	99.7%
1-Aminonaphthalene	ng/stk	20.9	0.145	2	0.0427	0.00513	3	0.2%	99.8%	0.3%	99.7%
2-Aminonaphthalene	ng/stk	17.5	0.497	2	0.0223	0.00321	3	0.1%	99.9%	0.2%	99.8%
3-Aminobiphenyl	ng/stk	4.60	0.137	2	0.0070	0.003	3	0.2%	99.8%	0.2%	99.8%
4-(Methyl-nitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	ng/stk	244.7	7.54	2	7.80	0.423	3	3.2%	96.8%	4.3%	95.7%
4-Aminobiphenyl	ng/stk	3.21	0.105	2	0.0087	0.0012	3	0.3%	99.7%	0.4%	99.6%
Acetaldehyde	µg/stk	1602	NA	1	192	11.6	3	12.0 %	88.0%	16.2%	83.8%
Acetamide	µg/stk	13.0	0.501	2	2.96	0.134	3	22.7 %	77.3%	30.7%	69.3%
Acetone	µg/stk	653	NA	1	30.7	1.86	3	4.7%	95.3%	6.4%	93.6%
Acrolein	µg/stk	158	NA	1	8.32	0.755	3	5.3%	94.7%	7.1%	92.9%
Acrylamide	µg/stk	4.50	0.294	2	1.58	0.0543	3	35.0 %	65.0%	47.3%	52.7%

HPHCs (alphabetic order)	Unit	3R4F			THS 2.2			% on stick basis		% on nicotine basis	
		mean	SD	n	mean	SD	n	% of 3R4F	% of reduction to 3R4F	% of 3R4F	% of reduction to 3R4F
Acrylonitrile	µg/stk	21.2	1.44	2	0.145	0.0112	3	0.7%	99.3%	0.9%	99.1%
Ammonia	µg/stk	33.2	0.539	2	12.2	0.973	3	36.8 %	63.2%	49.8%	50.2%
Arsenic	ng/stk	<7.49 (LOQ)	*	2	<0.36 (LOD)	*	3	NA	NA	NA	NA
Benz[a]anthracene	ng/stk	28.4	1.09	2	2.65	0.0647	3	9.3%	90.7%	12.6%	87.4%
Benzene	µg/stk	77.3	5.81	2	0.452	0.0395	3	0.6%	99.4%	0.8%	99.2%
Benzo[a]pyrene	ng/stk	13.3	0.660	2	0.736	0.0973	3	5.5%	94.5%	7.5%	92.5%
Butyraldehyde	µg/stk	81.3	NA	1	20.7	1.52	3	25.5 %	74.5%	34.5%	65.5%
Cadmium	ng/stk	89.2	9.31	2	<0.28 (LOQ)	*	3	<0.3 %	>99.7%	<0.4%	>99.6%
Carbon monoxide (CO)[1]	mg/stk	29.4	1.35	2	0.347	0.0462	3	1.2%	98.8%	1.6%	98.4%
Catechol	µg/stk	84.1	9.36	2	14.0	0.522	3	16.7 %	83.3%	22.5%	77.5%

[1] *CO is an ISO parameter but reported as HPHC in order to report the reduction to 3R4F*

HPHCs (alphabetic order)	Unit	3R4F			THS 2.2			% on stick basis		% on nicotine basis	
		mean	SD	n	mean	SD	n	% of 3R4F	% of reduction to 3R4F	% of 3R4F	% of reduction to 3R4F
Chromium	ng/stk	<11.9 (LOD)	*	2	<11.0 (LOQ)	*	3	NA	NA	NA	NA
Crotonaldehyde	µg/stk	49.3	NA	1	<3.29	*	3	<6.7 %	>93.3%	<9.0%	>91.0%
Dibenz[a,h]anthracene	ng/stk	<0.689 (LOQ)	*	2	<0.124 (LOD)	*	3	NA	NA	NA	NA
Ethylene oxide	µg/stk	16.0	1.18	2	<0.119 (LOQ)	*	3	<0.7 %	>99.3%	<1.0%	>99.0%
Formaldehyde	µg/stk	79.4	NA	1	14.1	0.430	3	17.8 %	82.2%	24.1%	75.9%
Hydrogen cyanide	µg/stk	329	16.2	2	<1.75 (LOQ)	*	3	<0.5 %	>99.5%	<0.7%	>99.3%
Hydroquinone	µg/stk	94.5	10.3	2	6.55	0.461	3	6.9%	93.1%	9.4%	90.6%
Isoprene	µg/stk	891	35.8	2	1.51	0.129	3	0.2%	99.8%	0.2%	99.8%
Lead	ng/stk	31.2	2.78	2	2.23	0.351	3	7.2%	92.8%	9.7%	90.3%
m-Cresol	µg/stk	4.24	0.461	2	0.0424	0.0045	3	1.0%	99.0%	1.4%	98.6%
Mercury	ng/stk	3.68	0.140	2	1.38	0.163	3	37.4 %	62.6%	50.6%	49.4%
Methyl-ethyl-ketone (MEK)	µg/stk	183	NA	1	10.1	0.759	3	5.5%	94.5%	7.4%	92.6%
Nickel	ng/stk	<12.9 (LOD)	*	2	<15.9 (LOQ)	*	3	NA	NA	NA	NA

HPHCs (alphabetic order)	Unit	3R4F			THS 2.2			% on stick basis		% on nicotine basis	
		mean	SD	n	mean	SD	n	% of 3R4F	% of reduction to 3R4F	% of 3R4F	% of reduction to 3R4F
Nitric oxide (NO)	µg/stk	484	7.20	2	12.6	0.418	3	2.6%	97.4%	3.5%	96.5%
Nitro benzene	µg/stk	<0.038 (LOD)	*	2	<0.011 (LOD)	*	3	NA	NA	NA	NA
Nitrogen oxides (NOx)	µg/stk	538	8.78	2	14.2	0.413	3	2.6%	97.4%	3.6%	96.4%
N-nitrosoanabasine (NAB)	ng/stk	29.0	1.08	2	2.35	0.0589	3	8.1%	91.9%	11.0%	89.0%
N-nitrosoanatabine (NAT)	ng/stk	254	17.4	2	14.7	1.25	3	5.8%	94.2%	7.9%	92.1%
N-Nitrosonornicotine (NNN)	ng/stk	271	8.49	2	10.1	0.205	3	3.7%	96.3%	5.0%	95.0%
o-Cresol	µg/stk	4.81	0.304	2	0.0779	0.0093	3	1.6%	98.4%	2.2%	97.8%
o-Toluidine	ng/stk	96.2	3.09	2	1.10	0.0243	3	1.1%	98.9%	1.5%	98.5%
p-Cresol	µg/stk	9.60	0.929	2	0.0706	0.00816	3	0.7%	99.3%	1.0%	99.0%
Phenol	µg/stk	15.6	1.75	2	1.47	0.206	3	9.4%	90.6%	12.7%	87.3%
Propionaldehyde	µg/stk	109	NA	1	10.8	0.675	3	9.9%	90.1%	13.4%	86.6%
Propylene oxide	ng/stk	896	82.5	2	142.3	6.67	3	15.9 %	84.1%	21.5%	78.5%
Pyrene	ng/stk	79.2	3.58	2	8.20	0.152	3	10.3 %	89.7%	14.0%	86.0%
Pyridine	µg/stk	30.9	1.64	2	6.58	0.185	3	21.3 %	78.7%	28.8%	71.2%

HPHCs (alphabetic order)	Unit	3R4F			THS 2.2			% on stick basis		% on nicotine basis	
		mean	SD	n	mean	SD	n	% of 3R4F	% of reduction to 3R4F	% of 3R4F	% of reduction to 3R4F
Quinoline	µg/stk	0.434	0.0246	2	<0.011 (LOQ)	*	3	<2.5 %	>97.5%	<3.4%	>96.6
Resorcinol	µg/stk	1.72	0.168	2	<0.055 (LOQ)	*	3	<3.2 %	>96.8%	<4.3%	>95.7
Selenium[2]	ng/stk	<4.42 (LOD)	*	2	1.27	0.0577	3	NA	NA	NA	NA
Styrene	µg/stk	13.9	1.72	2	0.577	0.0916	3	4.2%	95.8%	5.6%	94.4%
Toluene	µg/stk	129	1.17	2	1.42	0.162	3	1.1%	98.9%	1.5%	98.5%
Vinyl chloride	ng/stk	93.4	3.00	2	<0.657 (LOD)	*	3	<0.7 %	>99.3%	<1.0%	>99.0%

[2] In the case of selenium, the 3R4F is below the LOD while a value is reported for the THS. The LOD for 3R4F however, is higher than the value reported for the THS. In such a case the % of THS vs. 3R4F is impossible to estimate.

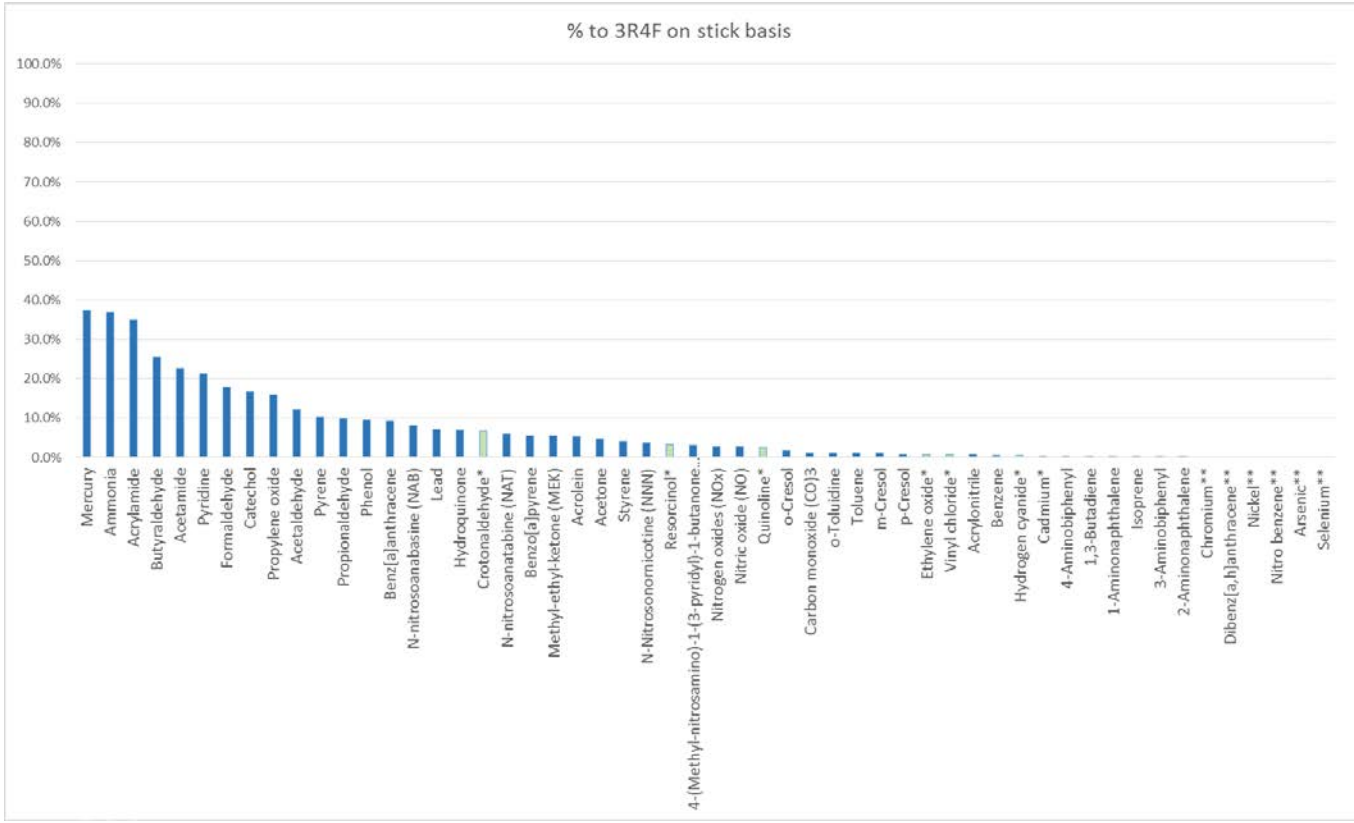


Figure 1: *HPHCs of THS 2.2 Regular vs. reference 3R4F cigarette. % on stick basis in decreasing order.*

HPHCs marked with a "" and identified with light color bars were reported below LOQ in THS 2.2 and relative % is based on LOQ. HPHCs marked with a "**" were found below LOQ in both reference and THS 2.2 and no relative % can be calculated (marked as NA in Table 3 above).*

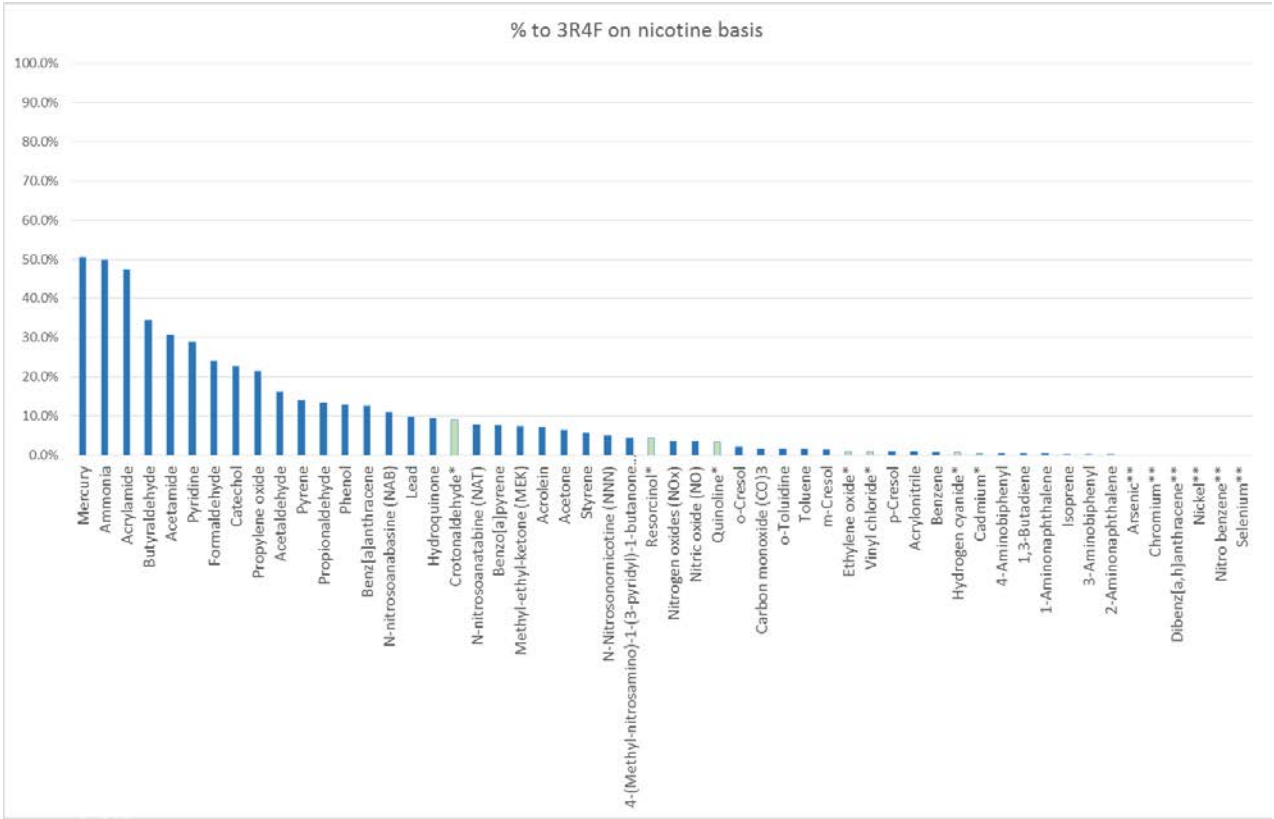


Figure 2: HPHCs of THS 2.2 Regular vs. reference 3R4F cigarette. % on nicotine basis in decreasing order.

HPHCs marked with a "" and identified with light color bars were reported below LOQ in THS 2.2 and relative % is based on LOQ. HPHCs marked with a "**" were found below LOQ in both reference and THS 2.2 and no relative % can be calculated (marked as NA in Table 3 above).*

Average reduction of HPHCs (not including main aerosol deliveries, TPM, nicotine, NFDPM, glycerin and water)

The average reduction is based on HPCHs reported in Table 3 and represent the average of column "% of reduction to 3R4F". The averages were calculated on stick basis and on nicotine basis:

- On stick basis : >92 %
- On nicotine basis : >89 %

7 Conclusions Data Evaluation

The total reduction of HPHCs of P1 Dorado II Ron vs. combustible reference cigarette 3R4F (not including nicotine, TPM, glycerin and water) was found to be >92 % on stick basis and >89 % on nicotine basis.

8 References

1. P1_THS 2.2_EXPT004923_Testing Protocol for Regulatory submission version 1.0, Kozikis Konstantin, Meyer Cedric, Moores Shelley, December 1st 2015
2. Analytical Test Report, NS308-H, Peter Joza, Labstat International ULC, April 13th 2016

9 Review

This document has been reviewed by:

Name	Function	Date / Signature
Jeannet Cyril	Singed as Author / Manager Product Characterization	7-Jun-2016
Maeder Serge	Signed as Owner and Approver / Director Testing Laboratories and Governance	7. Jun. 2016

10 Document versions

Version	Description	Change type
1.0	Initial version	NA
2.0	Reviewed reference section	Minor
3.0	Added LOD and LOQ values in the HPCH table 3	Minor
4.0	Reduction updated for Vinyl Chloride and graphs corrected accordingly	Minor