# THS 2.2 DORADO-I VINNY HIGH MENTHOL HPHCs COMPARISON TO COMBUSTIBLE REFERENCE PRODUCT 3R4F ANALYZED BY LABSTAT UCL

| | |
|---|---|
| PROGRAM NAME | THS 2.2 |
| PROJECT NAME | PRODUCT CHARACTERIZATION<br>DORADO-I Vinny High Menthol |
| WBS NUMBER | N/A |
| WORK PACKAGE NAME | N/A |
| EXPERIMENTAL WORK TYPE | Exploratory ☐<br>Developmental ☐<br>Regulatory submission ☒ |
| OWNER & APPROVER | SERGE MAEDER |
| AUTHOR | CYRIL JEANNET |
| DATE OF ISSUE | 23 September 2016 |

# Contents

1 Executive Summary ..... 3
2 Abbreviations ..... 3
3 Purpose ..... 5
4 Research Question ..... 5
5 Methods ..... 5
6 Results ..... 5
6.1 Data availability ..... 5
6.2 Results Dorado-I Vinny high Menthol ..... 6
7 Conclusions Data Evaluation ..... 15
8 References ..... 15
9 Review ..... 15
10 Document versions ..... 15

# Table of Tables

Table 1: Data considered in the present report ..... 5
Table 2: Main aerosol deliveries ..... 7
Table 3: HPCHs from the PMI-58 ..... 8

# Table of Figures

Figure 1: HPHCs of THS 2.2 Menthol vs. reference 3R4F cigarette. % on stick basis in decreasing order. ..... 12
Figure 2: HPHCs of THS 2.2 Menthol vs. reference 3R4F cigarette. % on nicotine basis in decreasing order. ..... 13

# 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 93% and 88% 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 |
| NO | Nitric Oxide |
| NOx | Nitrogen Oxides |

| Abbreviation/Term | Explanation |
|---|---|
| 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-12069

# 5 Methods

The detail of the analytical methodology is reported in the Labstat report [2] NS336-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* |
|---|---|---|---|
| B-27850 Batch of SMS.002543.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 I / CL / Menthol / Flavor Mint Vinny / T | 1682834 | SMP067927 | 3 replicates per sample |

## 6.2 Results Dorado-I Vinny high Menthol

Summary statistics and comparisons against the yields of the 3R4F reference combustible cigarette are presented in Table 2 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 Menthol | | |
|---|---|---|---|---|---|---|---|
| | | mean | SD | n | mean | SD | n |
| Glycerol[1] | mg/stk | 2.32 | * | 1 | 4.49 | 0.23 | 3 |
| Nicotine | mg/stk | 1.93 | * | 1 | 1.17 | 0.03 | 3 |
| Nicotine Free Dry Particulate Matter (NFDPM)[2] | mg/stk | 28.5 | * | 1 | 18.1 | 1.1 | 3 |
| Total Particulate Matter (TPM) | mg/stk | 44.9 | * | 1 | 55.3 | 0.83 | 3 |
| Water[3] | mg/stk | 14.5 | * | 1 | 36.0 | 0.49 | 3 |

**not possible to calculate SD as only one replicate was performed and reported by Labstat UCL*

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

[2] *We use here the ISO terminology NFDPM to describe the aerosol collected mass from THS 2.2. It should be noted that the NFDPM of the THS 2.2 has a very different constituent make-up in comparison to conventional cigarette. The glycerol, reported separately, is part of the NFDPM.*

[3] *The water value reported here was determined according to ISO 4387, and it is underestimated compared to the true value, due to important water losses linked with the high water content of the THS 2.2 aerosol. Accurate water measurements can only be obtained with a modified procedure, not available in Labstat [see 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 menthol | | | % 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 | 93.0 | 19.7 | 3 | 0.192 | 0.006 | 3 | 0.2% | 99.8% | 0.3% | 99.7% |
| 1-Aminonaphthalene | ng/stk | 21.7 | 0.7 | 3 | 0.060 | 0.003 | 3 | 0.3% | 99.7% | 0.5% | 99.5% |
| 2-Aminonaphthalene | ng/stk | 17.0 | 0.3 | 3 | 0.031 | 0.009 | 3 | 0.2% | 99.8% | 0.3% | 99.7% |
| 3-Aminobiphenyl | ng/stk | 4.51 | 0.14 | 3 | 0.009 | 0.001 | 3 | 0.2% | 99.8% | 0.3% | 99.7% |
| 4-(Methyl-nitrosamino)-1-(3-pyridyl)-1-butanone (NNK) | ng/stk | 282 | 28 | 3 | 5.52 | 0.34 | 3 | 2.0% | 98.0% | 3.2% | 96.8% |
| 4-Aminobiphenyl | ng/stk | 3.02 | 0.12 | 3 | 0.010 | 0.002 | 3 | 0.3% | 99.7% | 0.5% | 99.5% |
| Acetaldehyde | µg/stk | 1656 | 42.3 | 3 | 192 | 9 | 3 | 11.6% | 88.4% | 19.1% | 80.9% |
| Acetamide | µg/stk | 14.2 | 1.18 | 3 | 2.94 | 0.215 | 3 | 20.8% | 79.2% | 34.2% | 65.8% |
| Acetone | µg/stk | 658 | 14.3 | 3 | 38.7 | 2.29 | 3 | 5.9% | 94.1% | 9.7% | 90.3% |
| Acrolein | µg/stk | 161 | 5.22 | 3 | 9.32 | 0.569 | 3 | 5.8% | 94.2% | 9.5% | 90.5% |
| Acrylamide | µg/stk | 5.00 | 0.18 | 3 | 1.68 | 0.099 | 3 | 33.5% | 66.5% | 55.2% | 44.8% |
| Acrylonitrile | µg/stk | 23.5 | 4.0 | 3 | <0.107 (LOQ) | * | 3 | <0.5% | >99.5% | <0.7% | >99.3% |
| Ammonia | µg/stk | 26.7 | 3.7 | 2 | 10.7 | 0.943 | 3 | 40.1% | 59.9% | 66.0% | 34.0% |
| Arsenic | ng/stk | <7.49 (LOQ) | * | 3 | <1.20 (LOQ) | * | 3 | NA | NA | NA | NA |

| HPHCs (alphabetic order) | Unit | 3R4F | | | THS 2.2 menthol | | | % on stick basis | | % on nicotine basis | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | mean | SD | n | mean | SD | n | % of 3R4F | % of reduction to 3R4F | % of 3R4F | % of reduction to 3R4F |
| Benz[a]anthracene | ng/stk | 25.6 | 1.92 | 3 | 1.51 | 0.177 | 3 | 5.9% | 94.1% | 9.7% | 90.3% |
| Benzene | µg/stk | 73.5 | 10.1 | 3 | 0.473 | 0.036 | 3 | 0.6% | 99.4% | 1.1% | 98.9% |
| Benzo[a]pyrene | ng/stk | 14.4 | 1.08 | 3 | 0.448 | 0.073 | 3 | 3.1% | 96.9% | 5.1% | 94.9% |
| Butyraldehyde | µg/stk | 79.6 | 1.17 | 3 | 18.9 | 0.821 | 3 | 23.7% | 76.3% | 39.0% | 61.0% |
| Cadmium | ng/stk | 104 | 7.16 | 3 | 0.301 | 0.235 | 3 | 0.3% | 99.7% | 0.5% | 99.5% |
| Carbon monoxide (CO)[4] | mg/stk | 33.3 | * | 1 | 0.480 | 0.000 | 3 | 1.4% | 98.6% | 2.4% | 97.6% |
| Catechol | µg/stk | 101 | 4.48 | 3 | 14.1 | 0.211 | 3 | 14.0% | 86.0% | 23.1% | 76.9% |
| Chromium | ng/stk | <11.9 (LOD) | * | 3 | <11.0 (LOQ) | * | 3 | NA | NA | NA | NA |
| Crotonaldehyde | µg/stk | 49.9 | 1.13 | 3 | <3.29 (LOQ) | * | 3 | <6.6% | >93.4% | <10.9% | >89.1% |
| Dibenz[a,h]anthracene | ng/stk | 1.02 | 0.121 | 3 | <0.124 (LOD) | * | 3 | <12.1% | >87.9% | <20.0% | >80.0% |
| Ethylene oxide | µg/stk | 15.7 | 0.628 | 3 | 0.125 | 0.041 | 3 | 0.8% | 99.2% | 1.3% | 98.7% |

[4] *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 menthol | | | % on stick basis | | % on nicotine basis | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | mean | SD | n | mean | SD | n | % of 3R4F | % of reduction to 3R4F | % of 3R4F | % of reduction to 3R4F |
| Formaldehyde | µg/stk | 92.9 | 4.75 | 3 | 10.0 | 0.773 | 3 | 10.7% | 89.3% | 17.7% | 82.3% |
| Hydrogen cyanide | µg/stk | 378 | 13.0 | 3 | 2.71 | 0.191 | 3 | 0.7% | 99.3% | 1.2% | 98.8% |
| Hydroquinone | µg/stk | 92.9 | 8.47 | 3 | 6.48 | 0.220 | 3 | 7.0% | 93.0% | 11.5% | 88.5% |
| Isoprene | µg/stk | 927 | 88.6 | 3 | 1.27 | 0.281 | 3 | 0.1% | 99.9% | 0.2% | 99.8% |
| Lead | ng/stk | 30.2 | 0.459 | 3 | <1.62 (LOQ) | * | 3 | <5.4% | >94.6% | <8.8% | >91.2% |
| m-Cresol | µg/stk | 4.14 | 0.558 | 3 | <0.019 (LOQ) | * | 3 | <0.5% | >99.5% | <0.8% | >99.2% |
| Mercury | ng/stk | 4.13 | 0.283 | 2 | 1.89 | 0.066 | 3 | 45.6% | 54.4% | 75.2% | 24.8% |
| Methyl-ethyl-ketone (MEK) | µg/stk | 168 | 3.69 | 3 | 7.37 | 0.417 | 3 | 4.4% | 95.6% | 7.2% | 92.8% |
| Nickel | ng/stk | <12.9 (LOD) | * | 3 | <15.9 (LOD) | * | 3 | NA | NA | NA | NA |
| Nitric oxide (NO) | µg/stk | 471 | 36.5 | 3 | 12.8 | 1.04 | 3 | 2.7% | 97.3% | 4.5% | 95.5% |
| Nitro benzene | µg/stk | <0.038 (LOD) | * | 3 | <0.011 (LOD) | * | 3 | NA | NA | NA | NA |
| Nitrogen oxides (NOx) | µg/stk | 523 | 37.5 | 3 | 13.9 | 1.14 | 3 | 2.7% | 97.3% | 4.4% | 95.6% |
| N-nitrosoanabasine (NAB) | ng/stk | 33.9 | 1.03 | 3 | 2.19 | 0.442 | 3 | 6.5% | 93.5% | 10.6% | 89.4% |
| N-nitrosoanatabine (NAT) | ng/stk | 314 | 29.6 | 3 | 15.4 | 2.61 | 3 | 4.9% | 95.1% | 8.1% | 91.9% |
| N-Nitrosonornicotine (NNN) | ng/stk | 274 | 22.4 | 3 | 7.75 | 0.766 | 3 | 2.8% | 97.2% | 4.7% | 95.3% |

| HPHCs (alphabetic order) | Unit | 3R4F | | | THS 2.2 menthol | | | % on stick basis | | % on nicotine basis | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | mean | SD | n | mean | SD | n | % of 3R4F | % of reduction to 3R4F | % of 3R4F | % of reduction to 3R4F |
| o-Cresol | µg/stk | 4.98 | 0.525 | 3 | 0.043 | 0.005 | 3 | 0.9% | 99.1% | 1.4% | 98.6% |
| o-Toluidine | ng/stk | 106 | 3.14 | 3 | 0.982 | 0.083 | 3 | 0.9% | 99.1% | 1.5% | 98.5% |
| p-Cresol | µg/stk | 10.1 | 1.21 | 3 | <0.034 (LOQ) | * | 3 | <0.3% | >99.7% | <0.6% | >99.4% |
| Phenol | µg/stk | 16.7 | 1.39 | 3 | 0.927 | 0.072 | 3 | 5.5% | 94.5% | 9.1% | 90.9% |
| Propionaldehyde | µg/stk | 118 | 3.35 | 3 | 11.8 | 0.662 | 3 | 10.0% | 90.0% | 16.4% | 83.6% |
| Propylene oxide | ng/stk | 921 | 64.6 | 3 | 119 | 6.27 | 3 | 12.9% | 87.1% | 21.3% | 78.7% |
| Pyrene | ng/stk | 93.8 | 4.95 | 3 | 7.55 | 0.552 | 3 | 8.0% | 92.0% | 13.2% | 86.8% |
| Pyridine | µg/stk | 27.0 | 1.45 | 3 | 6.05 | 0.326 | 3 | 22.4% | 77.6% | 36.9% | 63.1% |
| Quinoline | µg/stk | 0.410 | 0.004 | 3 | <0.011 (LOQ) | * | 3 | <2.7% | >97.3% | <4.4% | >95.6% |
| Resorcinol | µg/stk | 1.93 | 0.130 | 3 | <0.055 (LOQ) | * | 3 | <2.9% | >97.1% | <4.7% | >95.3% |
| Selenium | ng/stk | <4.42 (LOD) | * | 3 | <0.83 (LOQ) | * | 3 | NA | NA | NA | NA |
| Styrene | µg/stk | 11.9 | 1.08 | 3 | 0.460 | 0.080 | 3 | 3.9% | 96.1% | 6.3% | 93.7% |
| Toluene | µg/stk | 119 | 8.39 | 3 | 1.03 | 0.272 | 3 | 0.9% | 99.1% | 1.4% | 98.6% |
| Vinyl chloride | ng/stk | 101 | 13.9 | 3 | <0.657 (LOD) | * | 3 | <0.7% | >99.3% | <1.1% | >98.9% |

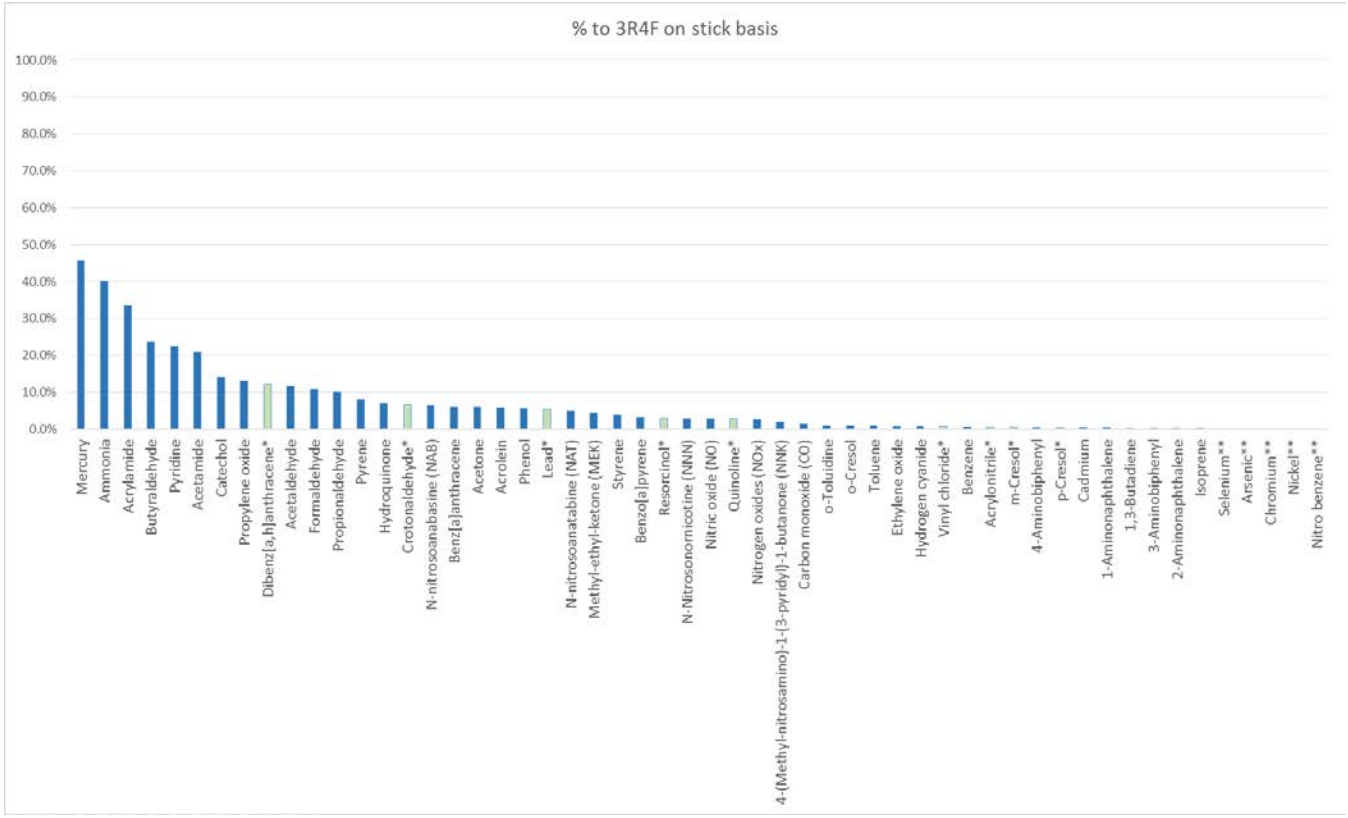



*Figure 1: HPHCs of THS 2.2 Menthol vs. reference 3R4F cigarette. % on stick basis in decreasing order.*
*HPHCs marked with a "*" and identified with light color bars were reported below LOQ in THS 2.2 and relative % is based on LOQ. HPHCs marked with a "**" were found below LOQ in both reference and THS 2.2 and no relative % can be calculated (marked as NA in Table 3 above).*

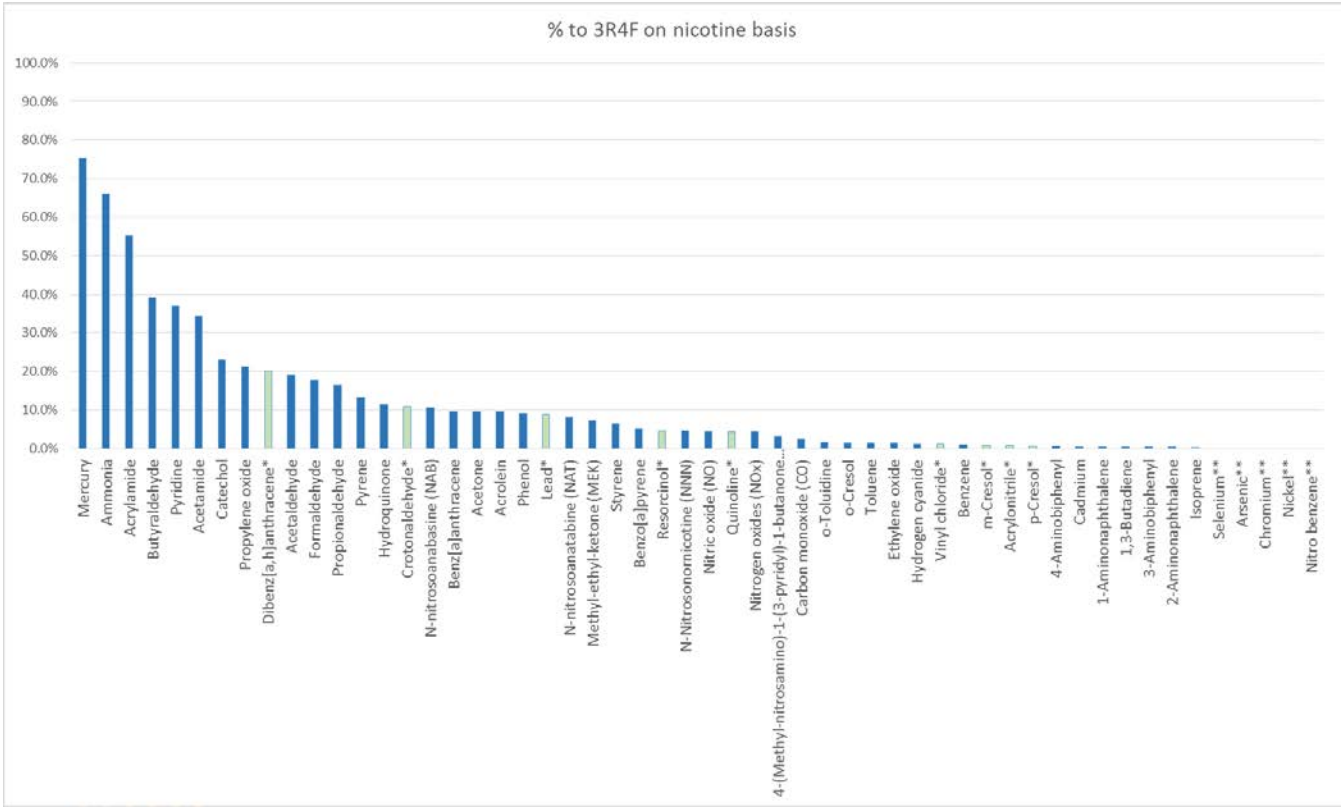



*Figure 2: HPHCs of THS 2.2 Menthol vs. reference 3R4F cigarette. % on nicotine basis in decreasing order.*

*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 : >93%
- On nicotine basis : >88%

## 7 Conclusions Data Evaluation

The total reduction of HPHCs of P1 Dorado I Vinny high menthol vs. combustible reference cigarette 3R4F (not including nicotine, TPM, glycerin and water) was found to be >93% on stick basis and >88% on nicotine basis.

## 8 References

1. P1_THS 2.2_EXPT004923_Testing Protocol for Regulatory submission version 3.0, Miller Beate, Minzoni Mirko, Moores Shelley, June 27st 2016
2. Analytical Test Report, NS336-H revision 1, Peter Joza, Labstat International ULC, September 21st 2016

## 9 Review

This document has been reviewed by:

| Name | Justification / Function | Date / Signature |
|---|---|---|
| Jeannet Cyril | Singed as Author / Manager Product Characterization | 23-Sep-2016 |
| Maeder Serge | Signed as Owner and Approver / Director Testing Laboratories and Governance | 23 Sep. 2016 |

## 10 Document versions

| Version | Description | Change type |
|---|---|---|
| 1.0 | Initial version | NA |