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Toxic Metal Concentrations in Mainstream Smoke from Cigarettes Available in the USA

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Abstract

Public health officials and leaders of 168 nations have signaled their concern regarding the health and economic impacts of smoking by becoming signatory parties to the World Health Organization Framework Convention on Tobacco Control (FCTC). One of FCTC's purposes is to help achieve meaningful regulation for tobacco products in order to decrease the exposure to harmful and potentially harmful constituents (HPHCs) delivered to users and those who are exposed to secondhand smoke. Determining baseline delivery ranges for HPHCs in modern commercial tobacco products is crucial information regulators could use to make informed decisions.

Establishing mainstream smoke delivery concentration ranges for toxic metals was conducted through analyses of total particulate matter (TPM) collected with smoking machines using standard smoking regimens.

We developed a rapid analytical method with microwave digestion of TPM samples obtained with smoking machines using electrostatic precipitation under the ISO and Intense smoking regimens. Digested samples are analyzed for chromium, manganese, cobalt, nickel, arsenic, cadmium, and lead using inductively coupled plasma-mass spectrometry. This method provides data obtained using the ISO smoking regimen for comparability with previous studies as well as an Intense smoking regimen that represents deliveries that fall within the range of human exposure levels to toxic metals.

Keywords

cigarette smoke; metals; cadmium; arsenic

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Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Introduction

The proportion of smokers in the US has decreased over the last forty years, though the number appears to have leveled off at approximately 19% of the adult population.[1,2] However, it is projected that total worldwide deaths from all smoking attributable diseases will increase from 5.4 million in 2004 to 8.3 million in 2030, reaching almost 10% of all deaths. Chronic obstructive pulmonary disease (COPD) alone is forecast to become the third leading cause of death worldwide by 2030, predominantly due to projected increases in smoking in developing countries.[3]

The initiation and progression of disease as a consequence of smoking may be attributed to the combined pathological impacts of more than 7,000 substances found in the complex tobacco smoke mixture. Due to the complexity involved in attempting to assess the individual contributions of these substances to the health risk from smoking, health risk estimates are generally based on the potential for exposures to multiple individual constituents or classes of constituents found in the smoke.[4] Fowles and Dybing broached the difficult task of assessing carcinogenic health risk from exposure to the substances found in tobacco smoke.[5] They assessed cancer risk indices from exposure to 40 substances for which cancer potency factors were available on an individual basis. They calculated cumulative lifetime exposure based on reports of average concentrations of toxicant transported in smoke per cigarette. They further assessed the additive risk from the substances as classes of toxic chemicals. Among the substances which contributed to the cancer risk from inhaling tobacco smoke are the toxic metals arsenic, beryllium, cadmium, chromium (VI), nickel (International Agency for Research on Cancer (IARC) group 1 carcinogens), and lead (IARC group 2A carcinogen). Burns et al. also considered assessing health risk due to exposure to substances in smoke as a basis for product regulation, but they based their calculations on toxicant delivery per mg of nicotine in smoke instead of per cigarette.[6] This provided justification and rationale for a regulation proposal by the WHO Study Group on Tobacco Product Regulation (TobReg) to lower toxicants in cigarette smoke. They also discussed the current scientific consensus that the International Organization for Standardization (ISO) smoking machine regimen (2000, 35 mL puff volume, 1 puff per minute, no ventilation blocking) is unsatisfactory for providing valid estimates of human exposure and for purposes of product regulation, as did Hammond et al.[6,7] Since much of the data available for calculating cancer risk indices were obtained using the ISO smoking regimen, Fowles and Dybing concluded that the cancer risk indices underestimate the observed cancer rates by about fivefold when using ISO yields in the exposure estimate.[5] Their conclusion is in agreement with the consensus statements of Burns et al.[5,6]

In addition to cancer risks, toxic metals may contribute to non-cancer health risks such as cardiovascular disease[8–10] and diseases such as COPD and smoking related interstitial lung disease that are characterized by sensitization, chronic inflammation, or tissue remodeling.[11–14] Fowles and Dybing calculated risk indices for the exposure to toxic substances in tobacco smoke that cause known non-cancer respiratory and cardiovascular health effects.[5] However, they pointed out that the magnitude of non-cancer risks were underestimated due to gaps in dose-response information and corresponding definitive threshold values from authoritative sources for many substances in smoke. The risk estimates were probably underestimated to an even greater degree due to the fact that much of the data available on which to base exposure was obtained from analyses of mainstream smoke collected using the ISO smoking machine regimen as previously mentioned.

In order to address the need for more data on toxic substances in smoke, information generated with smoking regimens that more closely approximate human exposure levels is important to fill these information gaps. Generally, TPM is collected from cigarettes that have been prepared under ISO 3402 (ISO 1999) conditions and smoked using the standard ISO smoking machine regimen (ISO 3308 and ISO 4387) or Health Canada Intense regimen (55 mL puff volume, 2 puffs per minute).[15–18] Analyses of TPM obtained from cigarettes that are conditioned and smoked according to the same standards can be used for comparing harmful and potentially harmful constituent (HPHC) deliveries from different brands of cigarettes and for establishing meaningful reference ranges for comparing relative smoke toxicant deliveries. However, the results obtained using standard regimens should not be misconstrued as absolutely representing all individual exposures from smoking, since the smoking habits differ for every individual.[6,7]

Here, we describe the development of a streamlined approach for analyzing tobacco smoke particulate for select toxic metals to determine the amounts of these metals (sensitizing agents, inflammatory agents, and carcinogens) that are transported in the mainstream smoke particulate matter from popular U.S. domestic cigarette brands.

Experimental

TPM Samples

Fifty cigarette brand varieties were purchased in 2011 from retail outlets in the greater metropolitan Atlanta area in Georgia, USA. Sampling was according to a geographical convenience plan, not necessarily intended for the purpose of establishing a nationwide market comparison. The samples were assigned unique identification numbers and logged into a database. Samples were stored in their original packaging until needed. Only authorized personnel had access to the samples.

Cigarettes were conditioned prior to smoking at 22 ± 2 °C and 60 ± 5 % relative humidity for a minimum of 48 hours, according to ISO method 3402.[16] Smoking conditions (i.e., puff profile, volume, duration and frequency, air flow, etc.) were selected in the Borgwaldt RM20H rotary smoking machine software settings according to ISO 3308[17] or Intense smoking regimen parameters.[18] Twenty, forty, or sixty cigarettes, depending on TPM yield, were smoked for each analysis when the ISO smoking regimen was used with the rotary smoking machine. Ten cigarettes per analysis were smoked for each TPM sample obtained using the Intense regimen. When the Intense regimen was used, ventilation-blocking cigarette holders were substituted for the standard cigarette holders used for the ISO regimen. The TPM was collected by electrostatic precipitation in preweighed high purity quartz tubes. Total TPM mass was determined as the difference between the end-capped quartz tube mass before and after smoking.

Sample, Quality Control, and Procedural Blank Preparation

TPM was transferred from quartz precipitation tubes to perfluoroalkoxy (PFA) lined high purity quartz digestion vessels with clean polystyrene spatulas (Fisher, Pittsburgh, PA, USA). Transferred mass was determined as the difference between vessel mass before and after TPM transfer. Transfer recovery was determined as TPM transferred / Total TPM mass. The TPM was digested with 7 mL Optima ultrapure nitric acid (ThermoFisher, Pittsburgh, PA, USA) in a Discover SPD+ sequential microwave system (CEM, Matthews, NC, USA) programmed with a 4 minute ramp to 200°C, then maintained at 200°C for 3 minutes. Transfer recovery factors were combined with conversion factors in the Agilent MassHunter software (Agilent Technologies, Tokyo, Japan) to convert ng/L diluted digestate concentrations to ng/cigarette. Approximately 5 mL nitric acid remaining after digestion and ventilation was diluted to 10 mL final volume.

Quality control (QC) TPM samples from 2R4F and 3R4F research reference cigarettes (University of Kentucky, Lexington, KY, USA) and CM6 cigarettes (Coresta, Paris, France) were obtained using the same procedure. The QC digestions were prepared for each analytical run. Procedural blanks were prepared by performing the digestion procedure in the PFA-lined digestion vessels with 7 mL nitric acid, and diluting as described for samples and QCs. Before analysis, aliquots from the 10 mL diluted digestates were further diluted to 1/10 with the internal standard diluent solution: 1.0 μg/L scandium, 1.0 μg/L iridium, 10 μg/L tellurium (internal standards) in 1% v/v ultrapure nitric acid, and 1.1% v/v 2-propanol (semiconductor grade VLSI, Sigma, St. Louis, MO, USA) prepared in ultrapure water. Samples collected for each cigarette variety were analyzed in seven analytical batches on seven different days, with 3R4F and CM6 run as QC samples each day.

ICP-MS Quantification

Five calibration standard solutions were prepared by dilution of High Purity Standards (HPS, Charleston, SC, USA) arsenic, cadmium, chromium, cobalt, manganese, nickel and National Institute for Standards and Technology lead standard SRM 981 (NIST, Gaithersburg, MD, USA). The calibration standards were prepared in 50% v/v ultrapure nitric acid, the acid concentration of diluted digested samples and QCs before addition of the internal standard diluent solution. Calibration ranges for all metals spanned the observed levels in the TPM digests. The following standard ranges (prior to dilution with internal standard solution), were recorded in the instrument software batches: ^{111}Cd, 10.00 to 150.0 μg/L; total Pb, 10.00 μg/L to 150.0 μg/L; ^{52}Cr, 0.100 to 1.500 μg/L; ^{55}Mn, 0.500 to 7.500 μg/L; ^{59}Co, 0.050 to 0.750 μg/L; ^{60}Ni, 0.500 to 7.500 μg/L; ^{75}As, 1.000 to 15.00 μg/L. Calibration was performed after 1/10 dilution of a calibration reagent blank and the five calibration standards in the internal standard diluent solution described above. Calibration curves for all metals had an $R \geq 0.995$.

Scandium (^{45}Sc) was assigned as the internal standard for chromium (^{52}Cr), manganese (^{55}Mn), cobalt (^{59}Co), and nickel (^{60}Ni). Tellurium (^{125}Te) was assigned as the internal standard for arsenic (^{75}As) and cadmium (^{111}Cd). Iridium (^{193}Ir) was assigned as internal standard for lead (Total Pb = $^{204}Pb + ^{206}Pb + ^{207}Pb + ^{208}Pb$, individually isotopically calibrated based on isotopic abundances of NIST SRM 981). The rinse solution between blanks, standards, and samples was 1% v/v ultrapure nitric acid with 1 μg/L tellurium (added to prevent memory effect and to maintain the equilibration of tellurium with the introduction system between samples).

Instrument Parameters

The Agilent 7700 ICP-MS was equipped with the following: ISIS valve and sample loop system for effective rinse between samples; ASX510 autosampler (Cetac, Omaha, NE, USA); low flow PFA nebulizer and Apex desolvating introduction system (Elemental scientific, Omaha, NE, USA); 0.44 mm I.D. pump tubing to enable 200 – 300 μL/min flow rates; and Platinum tipped cones. The Apex system was used without nitrogen addition. Ion intensity was integrated with peak hopping. Dwell times were 250 ms for all isotopes except ^{111}Cd, ^{193}Ir, and Pb isotopes. These isotopes were assigned dwell times of 100 ms.

The instrument was operated with standard 1550 watts RF power, 15 L/min argon plasma gas, and 0 L/min Dilution/Makeup gas. Carrier gas (sample gas) was optimized in the range of 0.97 to 1.00 L/min for < 0.3% cerium oxide formation while maintaining the highest possible signal intensity and stability. Sampling position, peristaltic pump speed, and other parameters were optimized with the same goals. Electrostatic lens parameters were optimized around Kinetic Energy Discrimination (KED) conditions (−18 V octapole bias, −15V quadrupole bias). Typical optimized cell gas flows were 5.5 mL/min helium and 0.5 mL/min hydrogen.

Quality Control

TPM QC results were monitored using SAS software (Cary, NC, USA.) The analytical QC samples were evaluated using a modified Westgard evaluation approach.[19] When a QC analyte was determined to be out of control according to the modified Westgard criteria, results for the failed analyte in the respective batch were not used and analyses were repeated.

Lowest Reportable Levels

The Procedural Detection Limits (LODs) were determined as follows:

$$LOD = [Mean_{procedural\ blank} + 1.645*(S_{procedural\ blank} + B)] / (1–1.645*A)$$ [21]

$Mean_{procedural\ blank}$ and $S_{procedural\ blank}$ were determined as the mean and total standard deviation from analyses of procedural digest blanks. Total standard deviations were calculated as follows:

$$S_T = 3 \times [S^2_{within\ run} + S^2_{between\ run}]^{1/2}.$$

$S_{within\ run}$ is the standard deviation from analysis of 20 separate procedural blanks in a single run. $S_{between\ run}$ is the standard deviation of the analysis of 60 separate procedural blanks in 60 separate runs.

Factors A (slope) and B (intercept) were determined according to Taylor,[20] by plotting between run standard deviation for the procedural blank, 2R4F, 3R4F, and CM6 versus their mean concentrations over 60 runs.

The Lowest Reportable Concentration Limit (LRL) was chosen from the higher of the LOD, or the concentration lowest calibration standard expressed in terms of ng/cigarette, whichever was higher. Lowest calibration standard concentration equivalents in ng/cigarette were obtained by multiplying the concentration by 0.010 L and dividing by 10 (Intense regimen), or 20 (ISO regimen) cigarettes smoked per run.

Statistical Analyses

Multivariate Statistical Analyses (MSA) of correlations between concentrations of metals that were transmitted into smoke were performed using JMP software (SAS, Cary, NC, USA). They were tabulated for arsenic, cadmium, and lead. They were not tabulated here for chromium, manganese, cobalt, and nickel, because of the low transported concentrations or significant number of results that were < LRL.

Results

Effect of Instrument Optimization on Accuracy

In preliminary data, the initially indicated helium cell gas flow optimum was 4.3 mL/min. While performance for 90% or more of the samples was adequate, occasional low level false positives for ^{52}Cr and ^{60}Ni were noted in a few TPM digests. Adding 0.5 mL/min hydrogen and increasing the helium flow to 5.5 mL/min eliminated the false positives. These cell conditions suppressed analyte signal to a greater degree, but avoiding false positive results was nevertheless advantageous with regard to the LRLs.

Analytical Results

The results from over 30 analyses of TPM obtained from reference cigarettes used as quality control samples using the ISO smoking regimen are comparable to other reported values (Table 2). The results of the heptuplicate analyses of TPM for seven toxic metals obtained from 50 varieties of cigarettes purchased in the greater Atlanta area using ISO and Intense smoking regimens were determined (Tables 3 and 4). The results from over 30 analyses of TPM obtained from reference cigarettes used as quality control samples using the Intense smoking regimen are also reported in Table 4.

Multivariate Statistical Analysis Results

MSA was performed to determine possible cigarette design parameters that were positively or negatively correlated with delivery of arsenic, cadmium, and lead, the metals that were transported at the three highest concentrations into smoke. The results for statistical analysis of correlation of cigarette physical design parameters with arsenic, cadmium, and lead delivery in both smoking regimens are included in Table 5.

Discussion

Effect of Instrument Optimization on Accuracy

In most cases, a combination of sample liquid and gas flows, optimization of sampling position, RF power, use of an appropriate nebulizer, and Peltier cooled or desolvating introduction systems, together with KED conditions, are sufficient for suppressing common interferences. However, there are a few interferences, such as when using employed.[22] Though we did not observe significant interferences when using KED with helium alone, the fact that chromium and nickel concentrations were near the LODs in all samples made even occasional minimal interferences undesirable. In the absence of hydrogen addition, occasional false positives for ^{52}Cr and ^{60}Ni were noted in a few diluted TPM digests. We did not determine the exact causes of the occasional low interferences, but low level argon ($^{36}Ar^{16}O$) and calcium ($^{44}Ca^{16}O$) oxides as described above were considered to be among the possibilities. The addition of hydrogen (0.5 mL/min) and increased helium flow rate (5.5 mL/min) eliminated even low concentration equivalent interferences, preventing false positive results.

Analytical Results: Reference Cigarettes

Our analyses of TPM obtained from 2R4F cigarettes for arsenic and lead using the ISO smoking regimen (Table 2) produced results that were comparable to those reported by Counts et al.[23] Our analyses of TPM obtained from 3R4F cigarettes for arsenic and lead using the ISO smoking regimen (Table 2) produced results that were comparable to those reported by Kuroki et al.[24] The mean result for arsenic determinations in TPM from 2R4F reported by three laboratories participating in an intercomparison study was 10.39 with 108% coefficient of variation. The mean lead result for 2R4F from four laboratories participating in an intercomparison study was 32.95 with 100% coefficient of variation.[25] The arsenic and lead data from these intercomparison studies are too scattered to be useful and thus are not mentioned here.

Our mean results for cadmium concentrations in TPM from 2R4F cigarettes were somewhat comparable to those of Counts et al.,[23] though approximately 11 ng per cigarette lower than those results. Our 3R4F results for cadmium, however, differed by approximately the same magnitude higher than the results of Kuroki et al.[24] Our cadmium results for 2R4F reference cigarettes were within one standard deviation below the mean results from four industry laboratories reported by Chen and Moldoveanu (47.8 ± 12.4 ng cadmium per cigarette).[25] There was greater variability between the respective laboratories for cadmium results. We noted that weekly cleaning of the syringe pump and daily cleaning of the cigarette holder tube bends in the rotary smoking machine dramatically decreased the variability of the cadmium and lead results. The greater dependence of these two analytes on machine maintenance could be related to their volatility relative to the other analytes.

Our chromium results were below reportable levels for both 2R4F and 3R4F, as were those of Counts et al. and Kuroki et al., respectively.[23,24] Chen and Moldoveanu reported a mean of 73.01 ng chromium per cigarette in TPM obtained from 2R4F from two participating laboratories.[25] The latter 2R4F value was probably due to either contamination or unresolved interferences.

Our nickel results were below reportable levels for both 2R4F and 3R4F, as were the 3R4F results of Kuroki et al.[24] One laboratory reported 5.12 ng nickel per cigarette for 2R4F in an intercomparison study.[25] We observed occasional false positives in this range when hydrogen was not used in the collision cell. Neither Counts et al. nor Kuroki et al. reported results for cobalt, manganese, or nickel. Chen and Moldoveanu also did not report cobalt or manganese results.

The results of our analyses of TPM obtained from the research cigarettes using the Intense smoking regimen are higher than the ISO values as expected (Table 4). Two-fold and four-fold greater concentrations of the respective metals in TPM were obtained using the Canada Intense regimen than in TPM obtained using the ISO regimen. We did not find published reports from other sources of metals analysis data from TPM obtained from 2R4F, 3R4F, or CM6 research cigarettes using the Intense regimen. We also reported data for the Coresta CM6 cigarette obtained using the ISO and Intense regimens (Tables 2, 4). We did not find other published results for metals concentrations in smoke particulate from the CM6 cigarette.

Study Cigarettes Results: ISO Smoking Regimen

Chromium concentrations were below the LRLs for all cigarettes when using the ISO smoking regimen (Table 3). Only 12% of TPM samples from all cigarette varieties had nickel concentrations above the LRL. Though chromium, manganese, and nickel concentrations in tobacco were higher than the concentrations of arsenic, cadmium, and lead;[26] arsenic, cadmium, and lead form more volatile metallic, chloride, or oxide species than chromium, manganese, and nickel. This is probably one of the reasons that the latter metals are not transported as efficiently in smoke.

The results of TPM analyses for other specific toxic metals obtained using the ISO smoking regimen follow the general expectation of the relationship between TPM transfer and cigarette filter ventilation. For example, arsenic, chromium, cobalt, and nickel concentrations in TPM obtained from Carlton White 100s, which may have in excess of 80% ventilation,[27] were lower than reportable levels. Concentrations of cadmium and lead in TPM obtained from Carlton White 100s using the ISO smoking regimen were the lowest of the 50 varieties analyzed. In like manner, Now Gold 100s, which have greater than 65% ventilation,[27] had the second lowest concentrations of arsenic, cadmium, cobalt, manganese, and lead. Marlboro (Red) 100s soft pack and Winston (Red) 100s hard pack, which may only have 10% ventilation,[27] had cadmium concentrations second only to the American Spirit Natural. TPM obtained from the three Newport varieties, which have little or no ventilation,[27] had the highest mean concentrations of cobalt when using the ISO smoking regimen. TPM from the Marlboro (Red) varieties, along with the Kool (Green) menthol varieties which may have no ventilation,[27] had the highest lead concentrations of the varieties analyzed in this study. Four of six metals were predicted to have significant impact from ventilation under ISO smoking conditions. Paper porosity was not predicted to have impact under ISO smoking conditions, probably due to the greater impact of filter ventilation.

Study Cigarettes Results: Intense Smoking Regimen

Chromium concentrations were below the LRLs for all cigarettes smoked using the Intense smoking regimen (Table 4). As a consequence of the more intense smoking parameters of the Health Canada Intense regimen,[7,18] TPM from 68% of the cigarette varieties had reportable nickel concentrations compared to only 12% of TPM samples of the cigarette varieties when smoked using ISO parameters. In addition to the greater puff volume (55 mL versus 35 mL) and greater puff frequency (every 30 seconds versus every 60 seconds) used for the Intense regimen, the greater transport of nickel (and other metals) in TPM could be attributed in large part to the filter ventilation blocking used in the Canada Intense regimen. Indeed, higher TPM delivery is observed for cigarettes smoked under Intense conditions than under ISO conditions.

American Spirit Natural cigarettes stood out with toxic metal concentrations at both the extreme high and low ends of the ranges for specific metals reported here. Tobacco filler from the American Spirit Natural cigarettes was previously reported to have lower mean cobalt and manganese concentrations than tobacco from other cigarettes.[26] Transport of cobalt and manganese in the smoke TPM obtained from these cigarettes using the Canada Intense regimen corresponded to filler concentrations that are the lowest and second lowest mean concentrations among the 50 varieties reported here. The filler from American Spirit also had the highest mean concentrations of cadmium and mercury.[26] The data from Table 4 show that transport of cadmium in the smoke TPM obtained from American Spirit Natural cigarettes using the Canada Intense regimen corresponded to filler cadmium concentrations that are the highest of all cigarettes in the study. Tobacco filler mean arsenic concentrations for American Spirit Natural cigarettes were among the top 14% of arsenic concentrations among the 50 varieties analyzed.[26] Arsenic concentrations in smoke TPM obtained from American Spirit cigarettes using the Canada Intense regimen corresponded to the relatively high filler arsenic concentrations that are the highest of the fifty varieties analyzed. Lead concentrations in smoke from American Spirit cigarettes were found to be the second lowest concentration among the 50 varieties analyzed. Accordingly, American Spirit tobacco filler was among the lowest 23 % of the tobacco filler lead concentrations previously reported.[26]

While there were correlations between toxic metal concentrations in tobacco filler and the concentrations in smoke TPM obtained using ISO smoking parameters, the correlations generally only held true for a given cigarette design. Filter ventilation in the cigarette design is a major factor in toxic metal transport especially when using the ISO regimen.[27] TPM transport, and thus toxic metal transport, is dependent upon the level of ventilation in the filter and the wrapping paper. Since the Health Canada Intense regimen specifies blocking the filter ventilation, toxic metal transport is less dependent on cigarette filter ventilation and more dependent on concentration in the tobacco. These are very important considerations for determining the health risk to the smoker. If a smoker decided to cut his or her exposure to TPM from smoke by changing the purchase choice from an unventilated to a more highly ventilated cigarette manufactured with identical tobacco, and smoking the same number of the more highly ventilated cigarettes per day with the identical puff frequency, puff profile, puff volume, and without covering ventilation holes with lips or fingers, then the smoker could in theory achieve a reduced exposure to TPM, though not necessarily to nicotine or other toxic substances. However, studies by Kozlowski and Pillitteri have shown that when smokers switch to a lower nicotine yield cigarette (generally a more highly ventilated cigarette), the majority of smokers compensate for the decreased nicotine delivery with more intense smoking habits.[28] Changes in smoking habits include: intentionally or unintentionally covering ventilation holes with lips or fingers, more frequent puffing, deeper puff volumes, or increasing the number of cigarettes smoked per day.

Burns et al. and Hammond et al. have expressed the current scientific consensus that the ISO smoking machine regimen is unsatisfactory for providing valid estimates of human exposure.[6,18] Hammond et al. added to the compensation studies of Kozlowski and Pilletteri[28] by showing that when smokers were given a low tar and nicotine delivery cigarette, they compensated with a mean smoke volume per cigarette of 802 mL, more than twice the inhaled smoke volume of the same cigarette smoked using the ISO regimen, and over 100 mL greater volume than the Massachusetts regimen, the Canadian intense regimen, and an experimental compensatory regimen.[18] This compensation volume was without regard to any intentional or unintentional ventilation blocking by participants. When regular yield brands were smoked by study participants, the participants inhaled somewhat smaller volumes than they inhaled with low tar and nicotine delivery cigarettes, but they still inhaled approximately twice the ISO regimen puff volume. They smoked with average intensities in terms of total smoke volume in the ranges of the Massachusetts and Canadian Intense regimens. This finding still permits a range of exposure possibilities, since for the same smoke volume, the cigarette burns more intensely with the Canada Intense regimen with 100% filter ventilation blocking than when using the Massachusetts regimen, for which filter ventilation is only 50% blocked. No smoking regimen is perfectly representative of the individual habits of all smokers. However, since the regular yield cigarettes would have little or no ventilation, it appears that the average puffing characteristics for smokers in the Hammond et al. study were far closer to the parameters of the Intense regimen than the ISO regimen.[18] Thus, the TPM exposure levels one would expect for a smoker who smokes with an average topography would be more accurately estimated from data obtained using the Canada Intense smoking regimen. The Intense smoking regimen provides useful information that may provide a closer approximation to human exposure, or at minimum, using the Intense regimen alongside the ISO regimen provides information that may bracket human exposure.

Statistical Analyses

The physical parameter that was most strongly correlated with delivery of arsenic, cadmium, and lead into smoke was tobacco weight per cigarette ($p < 0.0001$ for As and Cd in both smoking regimens, $p = 0.0011$ for Pb in ISO regimen, $p = 0.0002$ in Intense regimen). Higher tobacco mass per cigarette may be achieved by means of a longer portion of the cigarette rod packed with tobacco filler, or by tighter packing of a rod of given length. American Spirit Natural is an illustrative example of this correlation. This variety had the highest mean tobacco mass of the 50 varieties examined here (881 ± 44 mg per cigarette) as well as the highest mean arsenic and cadmium deliveries in both smoking regimens (Tables 3 and 4).

The cigarette rod length was strongly positively correlated with arsenic and lead delivery into smoke in both smoking regimens, but not with cadmium delivery (Tables 3 and 4). This may be due to the higher volatility of cadmium and may indicate that rod length is a more important determinant of the delivery of less volatile metals. Marlboro red hard pack 100s is an illustrative example of this correlation. This variety had 71 mm of the 100 mm rod devoted to tobacco content after subtracting the 29 mm filter length. This variety had the second highest mean arsenic delivery in both smoking regimens and the highest lead delivery in the Intense regimen (Tables 3 and 4).

Pressure drop shut, a measure of tightness of rod packing and also related to tobacco mass in a given rod length, was negatively correlated only with arsenic and lead delivery in the ISO smoking regimen.

Paper porosity was not significantly correlated with arsenic or lead delivery in either smoking regimen. Paper porosity was negatively correlated with cadmium delivery only in the ISO smoking regimen.

Filter ventilation was significantly negatively correlated with arsenic, cadmium, and lead deliveries in the ISO smoking regimen, as would be expected since the ventilation holes are unblocked. Filter ventilation is significantly negatively correlated only with cadmium delivery in the Intense smoking regimen. The latter case could also be due to the fact that filter length is often a greater proportion of the total rod length for ventilated cigarettes. Indeed filter length was correlated only with cadmium delivery in the Intense smoking regimen.

Most published data on smokers' exposure to toxic metals is based on deliveries using the ISO smoking regimen, which underestimates smoke inhalation of these HPHCs.[5,6,7,18] This paper therefore provides data that will be valuable for more accurate health risk assessments in keeping with the scientific consensus on estimating the smoke deliveries of toxic metals. Overall, using the Health Canada Intense smoking regimen, mainstream cigarette smoke metal levels yield data that more closely represents human exposure levels to toxic metals—data which could help enable more accurate estimates of cancer and non-cancer health risk indices.

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Table 1

Lower Reportable Limits (LRLs) (ng/cigarette)

Analyte	Intense Regimen (10 cigarettes) LRLs	ISO Regimen (20 cigarettes) LRLs
As	1.00	0.50
Cd	10.0	5.0
Co	0.050	0.025
Cr	1.1	0.88
Mn	0.50	0.25
Ni	0.50	0.38
Pb	10.0	5.0

Table 2

Comparing mean smoke metal concentration results from reference cigarettes using ISO smoking regimen with available results reported by others (ND: not determined).

ng/ cigarette	2R4F (CDC)	2R4F (Counts)[23]	3R4F (CDC)	3R4F (Kuroki)[24]	CM6 (CDC)
As	2.9 ± 0.4	3.3 ± 0.2	2.9 ± 0.3	2.7 ± 0.1	5.3 ± 0.5
Cd	40.2 ± 5.4	51.6 ± 2.1	38.8 ± 2.8	27.2 ± 0.9	80.2 ± 5.3
Co	0.051 ± 0.009	ND	0.049 ± 0.006	ND	0.065 ± 0.007
Cr	< 0.88	< 1.2	< 0.88	<0.87	< 0.88
Mn	1.1 ± 0.2	ND	1.0 ± 0.1	ND	1.1 ± 0.1
Ni	< 0.38	ND	< 0.38	< 0.59	0.48 ± 0.07
Pb	11.0 ± 1.1	13.0 ± 0.8	9.2 ± 0.7	9.6 ± 0.2	19.9 ± 1.1

Table 3

ISO Smoke Regimen Results (ng per cigarette)

ISO Smoke Regimen Results	As	Cd	Co	Cr	Mn	Ni	Pb
American Spirit Natural	5.8 ± 0.5	80 ± 3	0.052 ± 0.005	< 0.88	1.2 ± 0.1	< 0.38	12 ± 1
Basic Blue 100s HP	1.4 ± 0.1	20 ± 1	0.039 ± 0.002	< 0.88	0.66 ± 0.05	< 0.38	7.9 ± 0.3
Basic Gold 100s HP	2.8 ± 0.1	41 ± 2	0.074 ± 0.005	< 0.88	1.2 ± 0.1	< 0.38	18 ± 1
Basic Gold 100s SP	3.1 ± 0.5	38 ± 5	0.075 ± 0.008	< 0.88	1.3 ± 0.1	< 0.38	18 ± 2
Basic Green 100s HP Menthol	2.5 ± 0.3	31 ± 2	0.064 ± 0.002	< 0.88	1.2 ± 0.1	< 0.38	17 ± 1
Benson & Hedges Green 100s HP Menthol	3.7 ± 0.4	42 ± 4	0.071 ± 0.006	< 0.88	1.3 ± 0.1	< 0.38	19 ± 1
Benson & Hedges Luxury Gold 100s SP	2.9 ± 0.3	31 ± 2	0.053 ± 0.005	< 0.88	1.1 ± 0.1	< 0.38	15 ± 1
Camel Blue Turkish Domestic Blend HP	2.7 ± 0.4	34 ± 1	0.060 ± 0.004	< 0.88	1.2 ± 0.1	< 0.38	12 ± 1
Camel Turkish Domestic Blend HP	4.3 ± 0.3	43 ± 3	0.103 ± 0.049	< 0.88	2.0 ± 0.2	< 0.38	18 ± 2
Capri Magenta HP	2.9 ± 0.2	21 ± 2	0.069 ± 0.036	< 0.88	1.3 ± 0.1	< 0.38	9.7 ± 0.5
Carlton White 100s HP	< 0.50	< 5.0	< 0.025	< 0.88	< 0.25	< 0.38	< 5.0
Doral Gold HP	2.5 ± 0.2	35 ± 3	0.076 ± 0.010	< 0.88	1.4 ± 0.1	< 0.38	14 ± 1
Doral Silver 100s HP	1.5 ± 0.1	24 ± 2	0.037 ± 0.001	< 0.88	0.78 ± 0.07	< 0.38	7.4 ± 0.3
Kent Golden SP	2.2 ± 0.4	30 ± 6	0.051 ± 0.007	< 0.88	1.2 ± 0.2	< 0.38	10 ± 2
Kool Green Menthol HP	4.0 ± 0.5	42 ± 2	0.081 ± 0.005	< 0.88	1.8 ± 0.1	< 0.38	22 ± 1
Kool Green Menthol SP	4.0 ± 0.6	41 ± 3	0.076 ± 0.007	< 0.88	1.8 ± 0.1	< 0.38	21 ± 0
Marlboro Gold 100s HP	3.7 ± 0.3	37 ± 4	0.063 ± 0.005	< 0.88	1.2 ± 0.1	< 0.38	14 ± 1
Marlboro Gold 100s SP	3.5 ± 0.6	34 ± 2	0.059 ± 0.006	< 0.88	1.2 ± 0.2	< 0.38	14 ± 1
Marlboro Gold HP	3.7 ± 0.3	44 ± 2	0.061 ± 0.005	< 0.88	1.1 ± 0.1	< 0.38	14 ± 1
Marlboro Gold Menthol HP	3.0 ± 0.3	44 ± 3	0.063 ± 0.004	< 0.88	1.2 ± 0.1	< 0.38	13 ± 1
Marlboro Gold SP	3.6 ± 0.3	39 ± 4	0.059 ± 0.007	< 0.88	1.2 ± 0.2	< 0.38	15 ± 1
Marlboro Green Menthol HP	3.8 ± 0.4	44 ± 1	0.077 ± 0.008	< 0.88	1.5 ± 0.1	< 0.38	17 ± 1
Marlboro Red 100s HP	5.6 ± 0.4	45 ± 3	0.094 ± 0.007	< 0.88	1.9 ± 0.1	< 0.38	22 ± 1
Marlboro Red 100s SP	5.5 ± 0.3	51 ± 3	0.097 ± 0.008	< 0.88	1.9 ± 0.1	< 0.38	23 ± 1
Marlboro Red HP	5.3 ± 0.2	49 ± 2	0.086 ± 0.004	< 0.88	1.8 ± 0.1	0.46 ± 0.02	23 ± 1
Marlboro Red SP	5.3 ± 0.6	48 ± 3	0.087 ± 0.007	< 0.88	1.9 ± 0.1	0.44 ± 0.05	22 ± 2
Marlboro Red Label HP	4.2 ± 0.5	39 ± 2	0.067 ± 0.004	< 0.88	1.4 ± 0.1	< 0.38	16 ± 1

ISO Smoke Regimen Results	As	Cd	Co	Cr	Mn	Ni	Pb
Marlboro Silver 100s HP	1.9 ± 0.1	24 ± 2	0.038 ± 0.002	< 0.88	0.65 ± 0.06	< 0.38	8.0 ± 0.4
Marlboro Silver HP	1.9 ± 0.2	24 ± 2	0.032 ± 0.004	< 0.88	0.61 ± 0.05	< 0.38	7.6 ± 0.5
Maverick Gold 100s HP	2.8 ± 0.4	26 ± 4	0.075 ± 0.009	< 0.88	1.2 ± 0.1	< 0.38	9 ± 1
Merit Gold HP	1.9 ± 0.1	19 ± 1	0.043 ± 0.002	< 0.88	0.65 ± 0.04	< 0.38	9.2 ± 0.4
Misty Blue Slims	2.5 ± 0.2	29 ± 1	0.054 ± 0.007	< 0.88	1.1 ± 0.1	< 0.38	10 ± 1
Newport Green King SP Menthol	3.2 ± 0.2	50 ± 3	0.142 ± 0.009	< 0.88	1.9 ± 0.2	0.43 ± 0.02	17 ± 1
Newport Green Menthol 100s HP	3.3 ± 0.3	39 ± 3	0.151 ± 0.008	< 0.88	2.0 ± 0.1	< 0.38	15 ± 0
Newport Green Menthol HP	2.6 ± 0.2	42 ± 4	0.122 ± 0.007	< 0.88	1.9 ± 0.2	< 0.38	15 ± 1
Now Gold 100s SP	< 0.50	7.3 ± 0.9	0.015 ± 0.002	< 0.88	0.21 ± 0.03	< 0.38	1.8 ± 0.1
Pall Mall Blue	2.4 ± 0.2	33 ± 2	0.081 ± 0.007	< 0.88	1.3 ± 0.1	< 0.38	12 ± 1
Parliament Blue HP	2.3 ± 0.1	35 ± 3	0.053 ± 0.002	< 0.88	0.90 ± 0.08	< 0.38	12 ± 0
Salem Gold 100s	2.5 ± 0.2	28 ± 1	0.059 ± 0.006	< 0.88	1.3 ± 0.3	< 0.38	10 ± 1
Salem Gold HP	2.9 ± 0.4	42 ± 4	0.069 ± 0.006	< 0.88	1.2 ± 0.1	< 0.38	14 ± 1
Salem Green HP Menthol	4.6 ± 0.4	49 ± 2	0.103 ± 0.008	< 0.88	2.1 ± 0.2	0.48 ± 0.04	21 ± 2
Salem Silver 100s HP Menthol	1.4 ± 0.2	24 ± 4	0.035 ± 0.003	< 0.88	0.63 ± 0.08	< 0.38	6.2 ± 1.0
True Silver SP	0.9 ± 0.1	9.0 ± 1.0	0.030 ± 0.004	< 0.88	0.59 ± 0.06	< 0.38	< 5.0
USA Gold 100s SP	3.2 ± 0.5	51 ± 2	0.084 ± 0.005	< 0.88	1.4 ± 0.1	< 0.38	16 ± 1
Vantage SP	2.7 ± 0.2	38 ± 4	0.068 ± 0.007	< 0.88	1.4 ± 0.2	< 0.38	14 ± 1
Virginia Slims Gold 100s HP	2.6 ± 0.4	30 ± 3	0.056 ± 0.007	< 0.88	1.0 ± 0.1	< 0.38	13 ± 1
Winston Gold HP	2.8 ± 0.1	46 ± 4	0.081 ± 0.006	< 0.88	1.4 ± 0.1	< 0.38	12 ± 1
Winston Red 100s HP	4.4 ± 0.3	51 ± 2	0.093 ± 0.012	< 0.88	1.9 ± 0.1	0.44 ± 0.03	17 ± 1
Winston Red HP	4.6 ± 0.4	60 ± 2	0.110 ± 0.010	< 0.88	2.1 ± 0.1	0.46 ± 0.02	19 ± 1
Winston White 100s HP	1.5 ± 0.2	21 ± 2	0.033 ± 0.004	< 0.88	0.46 ± 0.09	< 0.38	5.2 ± 0.5
2R4F[§]	2.9 ± 0.4	40 ± 5	0.051 ± 0.009	< 0.88	1.1 ± 0.2	< 0.38	13 ± 1
3R4F[§]	2.9 ± 0.3	39 ± 3	0.049 ± 0.006	< 0.88	1.0 ± 0.1	< 0.38	9.2 ± 0.7
CM6[§]	5.3 ± 0.5	80 ± 5	0.065 ± 0.007	< 0.88	1.1 ± 0.1	0.48 ± 0.07	20 ± 1

[§]Data from > 30 analytical runs. All Brand names are trademarks of the respective manufacturers.

Table 4

Intense smoke regimen results (ng per cigarette).

Intense Smoke Regimen Results	As	Cd	Co	Cr	Mn	Ni	Pb
American Spirit Natural	15.2 ± 1.3	200 ± 12	0.09 ± 0.01	< 1.1	2.2 ± 0.2	*	29 ± 1
Basic Blue 100s HP	6.3 ± 1.2	94 ± 16	0.14 ± 0.02	< 1.1	2.8 ± 0.3	*	41 ± 3
Basic Gold 100s HP	7.9 ± 0.6	107 ± 9	0.16 ± 0.01	< 1.1	3.2 ± 0.2	0.62 ± 0.08	47 ± 3
Basic Gold 100s SP	7.6 ± 0.4	108 ± 9	0.16 ± 0.04	< 1.1	3.1 ± 0.3	0.69 ± 0.08	45 ± 3
Basic Green 100s HP Menthol	8.2 ± 0.9	105 ± 28	0.18 ± 0.03	< 1.1	3.0 ± 0.2	0.65 ± 0.12	46 ± 2
Benson & Hedges Green 100s HP Menthol	11.4 ± 1.3	129 ± 12	0.17 ± 0.01	< 1.1	3.2 ± 0.5	0.64 ± 0.13	58 ± 3
Benson & Hedges Luxury Gold 100s SP	9.3 ± 1.2	117 ± 16	0.15 ± 0.02	< 1.1	2.8 ± 0.4	*	46 ± 4
Camel Blue Turkish Domestic Blend HP	7.6 ± 0.4	113 ± 33	0.13 ± 0.01	< 1.1	3.1 ± 0.2	0.75 ± 0.28	32 ± 3
Camel Turkish Domestic Blend HP	9.9 ± 1.0	126 ± 12	0.18 ± 0.06	< 1.1	4.1 ± 0.4	0.88 ± 0.13	40 ± 3
Capri Magenta HP	9.1 ± 0.8	82 ± 9	0.15 ± 0.01	< 1.1	3.4 ± 0.2	0.89 ± 0.13	29 ± 1
Carlton White 100s HP	4.9 ± 0.7	91 ± 11	0.12 ± 0.04	< 1.1	2.7 ± 0.4	*	28 ± 3
Doral Gold HP	6.4 ± 0.4	81 ± 4	0.16 ± 0.03	< 1.1	3.6 ± 0.3	*	32 ± 3
Doral Silver 100s HP	6.3 ± 0.2	113 ± 8	0.15 ± 0.02	< 1.1	3.5 ± 0.3	0.70 ± 0.07	37 ± 4
Kent Golden SP	7.2 ± 0.4	101 ± 7	0.13 ± 0.01	< 1.1	3.1 ± 0.2	*	28 ± 2
Kool Green Menthol HP	10.7 ± 1.0	109 ± 10	0.19 ± 0.04	< 1.1	3.9 ± 0.6	0.90 ± 0.23	53 ± 5
Kool Green Menthol SP	9.7 ± 0.8	133 ± 9	0.19 ± 0.03	< 1.1	4.6 ± 0.4	0.82 ± 0.08	52 ± 2
Marlboro Gold 100s HP	10.8 ± 1.4	118 ± 7	0.14 ± 0.04	< 1.1	3.3 ± 0.4	0.82 ± 0.16	43 ± 3
Marlboro Gold 100s SP	12.1 ± 1.6	132 ± 11	0.16 ± 0.03	< 1.1	3.9 ± 0.3	0.78 ± 0.17	51 ± 5
Marlboro Gold HP	10.4 ± 0.3	128 ± 10	0.15 ± 0.03	< 1.1	3.3 ± 0.3	0.72 ± 0.06	44 ± 5
Marlboro Gold Menthol HP	8.5 ± 0.7	114 ± 15	0.14 ± 0.02	< 1.1	3.0 ± 0.4	0.63 ± 0.11	37 ± 2
Marlboro Gold SP	9.4 ± 1.8	123 ± 16	0.12 ± 0.06	< 1.1	2.7 ± 0.8	*	45 ± 7
Marlboro Green Menthol HP	12.3 ± 3.8	123 ± 18	0.16 ± 0.01	< 1.1	3.2 ± 0.4	0.76 ± 0.16	43 ± 3
Marlboro Red 100s HP	13.9 ± 0.7	154 ± 8	0.21 ± 0.03	< 1.1	4.7 ± 0.5	1.06 ± 0.20	57 ± 4
Marlboro Red 100s SP	12.8 ± 1.1	135 ± 17	0.18 ± 0.03	< 1.1	4.1 ± 0.7	1.00 ± 0.18	50 ± 5
Marlboro Red HP	12.1 ± 0.5	140 ± 7	0.19 ± 0.05	< 1.1	4.0 ± 0.2	0.92 ± 0.06	50 ± 4
Marlboro Red SP	13.1 ± 0.5	151 ± 3	0.20 ± 0.02	< 1.1	4.3 ± 0.3	1.03 ± 0.10	55 ± 3
Marlboro Red Label HP	11.2 ± 1.1	129 ± 15	0.19 ± 0.04	< 1.1	3.8 ± 0.6	0.87 ± 0.30	44 ± 6

Intense Smoke Regimen Results	As	Cd	Co	Cr	Mn	Ni	Pb
Marlboro Silver 100s HP	8.1 ± 1.0	112 ± 16	0.13 ± 0.02	< 1.1	2.6 ± 0.3	*	35 ± 3
Marlboro Silver HP	8.4 ± 0.8	99 ± 16	0.13 ± 0.04	< 1.1	2.7 ± 0.5	*	34 ± 3
Maverick Gold 100s HP	10.2 ± 0.9	103 ± 5	0.22 ± 0.05	< 1.1	4.3 ± 0.3	0.95 ± 0.15	33 ± 3
Merit Gold HP	5.7 ± 0.6	109 ± 11	0.12 ± 0.03	< 1.1	2.1 ± 0.2	*	35 ± 4
Misty Blue Slims	8.1 ± 1.1	85 ± 21	0.17 ± 0.03	< 1.1	3.2 ± 0.4	0.77 ± 0.13	33 ± 2
Newport Green King SP Menthol	7.3 ± 1.4	120 ± 31	0.27 ± 0.04	< 1.1	3.8 ± 0.6	*	35 ± 8
Newport Green Menthol 100s HP	7.3 ± 1.9	114 ± 19	0.30 ± 0.09	< 1.1	3.9 ± 0.8	0.88 ± 0.22	32 ± 6
Newport Green Menthol HP	7.3 ± 1.5	125 ± 14	0.27 ± 0.08	< 1.1	4.1 ± 0.7	0.90 ± 0.17	32 ± 5
Now Gold 100s SP	4.9 ± 0.9	91 ± 9	0.14 ± 0.01	< 1.1	2.3 ± 0.2	*	26 ± 2
Pall Mall Blue	8.8 ± 1.0	125 ± 12	0.21 ± 0.04	< 1.1	4.4 ± 0.6	1.04 ± 0.14	38 ± 6
Parliament Blue HP	6.5 ± 0.2	90 ± 7	0.13 ± 0.01	< 1.1	2.5 ± 0.2	*	33 ± 1
Salem Gold 100s	8.9 ± 0.6	129 ± 4	0.18 ± 0.03	< 1.1	3.9 ± 0.3	0.92 ± 0.07	41 ± 4
Salem Gold HP	8.0 ± 0.7	114 ± 9	0.19 ± 0.04	< 1.1	3.9 ± 1.1	0.87 ± 0.16	38 ± 7
Salem Green HP Menthol	10.5 ± 1.1	130 ± 9	0.22 ± 0.05	< 1.1	4.7 ± 0.5	1.09 ± 0.22	52 ± 3
Salem Silver 100s HP Menthol	6.8 ± 0.8	127 ± 12	0.15 ± 0.04	< 1.1	3.4 ± 0.2	0.70 ± 0.13	36 ± 3
True Silver SP	6.6 ± 0.7	88 ± 7	0.22 ± 0.02	< 1.1	4.0 ± 1.0	0.88 ± 0.10	32 ± 3
USA Gold 100s SP	8.4 ± 0.4	95 ± 5	0.20 ± 0.02	< 1.1	3.2 ± 0.2	*	40 ± 2
Vantage SP	7.6 ± 0.5	112 ± 16	0.15 ± 0.01	< 1.1	3.4 ± 0.4	*	42 ± 6
Virginia Slims Gold 100s HP	8.1 ± 0.7	94 ± 13	0.14 ± 0.02	< 1.1	2.6 ± 0.2	*	43 ± 3
Winston Gold HP	9.0 ± 0.7	140 ± 25	0.24 ± 0.03	< 1.1	3.8 ± 0.6	1.04 ± 0.25	37 ± 7
Winston Red 100s HP	10.4 ± 2.3	150 ± 16	0.20 ± 0.04	< 1.1	4.3 ± 0.3	1.01 ± 0.20	44 ± 4
Winston Red HP	8.5 ± 2.5	142 ± 35	0.17 ± 0.04	< 1.1	3.8 ± 1.0	0.94 ± 0.16	40 ± 10
Winston White 100s HP	7.9 ± 1.5	132 ± 12	0.16 ± 0.04	< 1.1	3.5 ± 0.4	0.84 ± 0.18	34 ± 3
2R4F[§]	9.9 ± 0.8	168 ± 18	0.17 ± 0.04	< 1.1	3.6 ± 0.4	0.76 ± 0.13	41 ± 5
3R4F[§]	9.9 ± 0.9	152 ± 15	0.15 ± 0.02	< 1.1	3.2 ± 0.3	0.75 ± 0.12	35 ± 2
CM6[§]	10.9 ± 0.9	176 ± 15	0.10 ± 0.02	< 1.1	1.9 ± 0.2	0.76 ± 0.14	41 ± 3

[*] One or more of the heptuplicate results was < 0.50 ng/cigarette.

[§] Data from > 30 analytical runs. All brand names are trademarks of the respective manufacturers.

Table 5

Multivariate Statistical Analysis Results for As, Cd, and Pb

Physical Parameters - Intense Regimen						
	Arsenic		Cadmium		Lead	
Parameter	**t ratio**	**p**	**t ratio**	**p**	**t ratio**	**p**
Rod Length	2.97	0.0031	0.37	0.7092	5.68	<0.0001
Filter Length	−0.43	0.6697	3.18	0.0016	−0.32	0.7496
% Tip Ventilation	−1.28	0.1999	−2.93	0.0037	−0.99	0.3214
Paper Porosity	1.88	0.0608	−1.23	0.2199	−1.37	0.1725
Tobacco Weight	6.49	<0.0001	5.2	<0.0001	3.78	0.0002
Pressure Drop Shut	−0.95	0.3428	1.89	0.0600	2.6259	0.1061

Physical Parameters - ISO Regimen						
	Arsenic		Cadmium		Lead	
Parameter	**t ratio**	**p**	**t ratio**	**p**	**t ratio**	**p**
Rod Length	4.7	<0.0001	−0.96	0.3402	4.52	<0.0001
Filter Length	−1.66	0.0950	−0.09	0.9288	−0.94	0.3460
% Tip Ventilation	−3.32	0.0010	−3.62	0.0003	−2.54	0.0116
Paper Porosity	0.38	0.7011	−2.7	0.0074	0.89	0.3716
Tobacco Weight	6.38	<0.0001	4.39	<0.0001	3.29	0.0011
Pressure Drop Shut	−2.09	0.0373	−1.85	0.0648	−3.11	0.0020